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(54) **Nebulizing catheter system and method of manufacture**

Katheter mit Zerstäubungseinrichtung sowie Verfahren zu seiner Herstellung

Cathéter comprenant un dispositif de nébulisation et son procédé de fabrication

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(56) References cited:
WO-A-87/05522
WO-A-93/17744
GB-A- 2 268 286
US-A- 5 031 613
US-A- 5 167 622
WO-A-90/07951
FR-A- 2 569 114
US-A- 4 739 756
US-A- 5 078 131

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Description

BACKGROUND OF THE INVENTION

[0001] The present invention relates to aerosol delivery of medication, and more particularly, but not exclusively, the present invention relates to delivery systems for application of nebulized medication to the lungs with improved delivery rates, efficiencies, and control.

[0002] Many types of medication can be administered to a patient via the respiratory tract. Medication delivered through the respiratory tract may be carried with a patient's inhalation breath as airborne particles (e.g. an aerosol or nebula) into the lungs where the medication can cross through the thin membrane of the alveoli and enter the patient's bloodstream. Delivery of medication via the respiratory tract may be preferred in many circumstances because medication delivered this way enters the bloodstream very rapidly. Delivery of medication to the lungs may also be preferred when the medication is used in a treatment of a disease or condition affecting the lungs in order to apply or target the medication as close as physically possible to the diseased area. Although delivery of medication via the respiratory tract has been used for many years, there are difficulties associated with prior systems that have limited their use and application. For example, conventional methods have provided for only limited medication delivery rates, efficiency, and control. Conventional methods for aerosol delivery result in a substantial portion of the medicine failing to be delivered to the lungs, and thereby possibly being wasted, or possibly being delivered to other parts of the body, e.g. the trachea.

[0003] Aerosols in general are relatively short-lived and can settle out into larger particles or droplets relatively quickly. Aerosols can also impact each other or other objects, settle out as sediment, diffuse, or coalesce. Aerosol particles can also be subject to hydroscopic growth as they travel. Delivery of medicine as airborne particles requires conversion of the medicine, which may be in liquid form, to an aerosol followed relatively quickly by application of the aerosol to the respiratory tract. One such device that has been utilized for this purpose is an inhaler. Inhalers may atomize a liquid to form an aerosol which a person inhales via the mouth or nose. Inhalers typically provide only limited delivery of medication to the lungs since most of the medication is deposited on the linings of the respiratory tract. It is estimated that as little as 10-15 % of an aerosol inhaled in this way reaches the alveoli.

[0004] Aerosol delivery of a medication to a patient's respiratory tract also may be performed while the patient is intubated, i.e. when an endotracheal tube is positioned in the patient's trachea to assist in breathing. When an endotracheal tube is positioned in a patient, a proximal end of the endotracheal tube may be connected to a mechanical ventilator and the distal end is located in the trachea. An aerosol may be added to the airflow in the ventilator circuit of the endotracheal tube and carried by the patient's inhalation to the lungs. A significant amount of the aerosolized medication may be deposited inside the endotracheal tube and the delivery rate of the medicine to the lungs also remains relatively low and unpredictable.

[0005] US-A-4 739 756 discloses an endotracheal tube adapted to deliver an aerosol to a patient's lungs. Multiple orifices are arranged around the distal end of a ventilation lumen and are in communication with a single medicament supply lumen.

[0006] The low and unpredictable delivery rates of prior aerosol delivery systems have limited the types of medications that are delivered via the respiratory tract. For new medications that are relatively expensive, the amount of wasted medicine may be a significant cost factor in the price of the therapy. Therefore, it would be advantageous to increase the delivery rate or efficiency of a medicine delivered to the lungs.

[0007] Another consideration is that some aerosols delivered to the lungs may have adverse side effects, e.g. radioactive tracers used for lung scans. Therefore, it would be advantageous to minimize the overall amount of medication delivered while maintaining the efficacy of the medication by providing the same or a greater amount of the medication to the desired site in the respiratory tract.

[0008] Further, some medications may be more effective when delivered in certain particle sizes. Accordingly, an improved aerosol delivery system may provide for improved rates and efficiencies of delivery also taking into account the aerosol particle size.

[0009] It may also be important to administer certain medications in specific, controlled dosages. The prior methods of aerosol delivery not only were inefficient, but also did not provide a reliable means to control precisely the dosage being delivered.

[0010] It may also be advantageous to be able to target medication to a specific bronchus, or specific groups of bronchia, as desired, while avoiding delivery of medication to other portions of the lungs.

[0011] Taking into account these and other considerations, aerosol delivery via the respiratory tract could become an even more widely used and effective means of medication delivery if the delivery rate and efficiency of the delivery could be improved.

SUMMARY OF THE INVENTION

[0012] According to an aspect of the present invention, there is provided an apparatus for delivering a drug with control and efficiency to a patient via the patient's respiratory system. According to first aspect of the invention there is provided a catheter for delivering an aerosol of medicine to a patient's lungs, the catheter comprising a catheter shaft having a liquid lumen centrally located in said shaft and adapted for conveying a medicine in liquid form; a plurality of gas lumens peripherally

located around said liquid lumen and adapted for conveying a gas; a distal liquid orifice communicating with said liquid lumen; and, a plurality of distal gas orifices communicating with said plurality of gas lumens, said plurality of gas orifices being aligned with respect to said distal liquid orifice so as to nebulize a liquid medicine discharged from the liquid orifice.

[0013] The nebulization catheter is positioned in the patient's respiratory system so that a distal end of the nebulization catheter is in the respiratory system and a proximal end is outside the body. The nebulization catheter may be used in conjunction with an endotracheal tube and preferably is removable from the endotracheal tube. The nebulization catheter conveys medicine in liquid form to the distal end at which location the medicine is nebulized by a pressurized gas or other nebulizing agent. The nebulized medicine is conveyed to the patient's lungs by the patient's respiration which may be assisted by a ventilator. The nebulizing catheter incorporates alternative constructions taking into account anatomical considerations and the properties of the medicine being nebulized to provide delivery of medicine with control and efficiency.

[0014] The invention further resides in a method of manufacturing a catheter as specified above but having a tapering distal tip region, the catheter having closely spaced distal orifices sized and spaced apart with low tolerances, and the method comprising the steps of:

providing a relatively large size multilumen extruded polymer tubing;
heating a portion of the tubing to a transition temperature of said tubing;
drawing down said portion of tubing to form a tapered section with a draw down ratio in the range between 2 to 1 and 20 to 1 such that the lumens are increasingly closely spaced in said tapered region; and,
forming a plurality of orifices at a distal end of said tapered section, said plurality of orifices being sized to nebulize a liquid delivered through one of said lumens to form an aerosol with a gas delivered through others of said lumens.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015]

FIG. 1 shows an exploded view of a first embodiment of the present invention.

FIG. 2 shows an assembled view of the embodiment of FIG. 1.

FIG. 2A is a sectional view of the nebulization catheter of FIGS. 1 and 2.

FIG. 3 is a plan view of an alternative embodiment of the endotracheal tube shown in FIGS. 1 and 2.

FIG. 4 is a cross sectional view taken along the line a-a' of the alternative embodiment of the endotracheal tube shown in FIG. 3 without the nebulizing catheter in place.

FIG. 5 is a cross sectional view taken along the line b-b' of the alternative embodiment of the endotracheal tube shown in FIG. 3 with the nebulizing catheter in place.

FIG. 6 is a plan view of an embodiment of the nebulizing catheter of FIGS. 1 and 2 shown in place in the trachea of a patient who is not intubated.

FIG. 7 is a perspective view of a distal end of an alternative nebulization catheter in accordance with an example of the invention.

FIG. 8 is a perspective view of an alternative embodiment of FIG. 7 with the liquid lumen shown in a closed condition.

FIG. 9 is a perspective view of the embodiment of FIG. 8 with the liquid lumen shown in an open condition.

FIG. 10 is a perspective view of a distal end of an alternative nebulization catheter in accordance with an example of the invention.

FIG. 11 is a perspective view of a distal end of another alternative nebulization catheter in accordance with an example of the invention.

FIG. 12 is a perspective view of a distal end of a further alternative nebulization catheter in accordance with an example of the invention.

FIG. 13 is a perspective view of a distal end of another alternative nebulization catheter in accordance with an example of the invention.

FIG. 14 is a perspective view of a distal end of a further alternative nebulization catheter in accordance with an example of the invention.

FIG. 15 is a perspective view of an alternative catheter which may embody the invention and which has a centering device.

FIG 16 is a side view of the catheter of FIG 15 embodying an alternative centering device.

FIG. 17 is a side view of the catheter of FIG 15 embodying a further alternative centering device.

FIG. 16 is a side view of the catheter of FIG 15 embodying yet another alternative centering device.

FIG. 19 is a side view of the catheter of FIG. 18 shown in another stage of operation.

FIG. 20 is a side view of a distal end of a nebulization catheter positioned in a patient's trachea illustrating an undesirable condition.

FIG. 21 is a perspective view similar to that of FIG. 20 of alternative catheter and endotracheal tube addressing the condition shown in FIG. 20.

FIG. 22 shows an alternative catheter and endotracheal tube in accordance with an example of the invention, positioned in a patient's trachea.

FIG. 23 shows an alternative catheter in accordance with an example of the invention.

FIG. 24 is a diagram illustrating a drug reservoir and pressurization assembly.

FIG. 25 is a diagram similar to that of FIG. 24 illustrating an alternative drug reservoir and pressurization assembly.

FIG. 26 is a sectional view along line c-c' of FIG. 25.

FIG. 27 is a side view of flow delivery system for a catheter including an optional humidification and heating arrangement.

FIG. 28 is a side view of a flow control system used in connection with a catheter for pressuring the liquid flow lumen.

FIG. 29 is a view similar to that of FIG. 28 showing the flow control system of FIG. 28 in another stage of operation.

FIG. 30 is a perspective view illustrating an entire nebulization catheter system including sensors.

FIG. 31 shows a sectional view of a catheter embodying an example of the invention and including a sensor.

FIG. 32 shows an alternative embodiment of the catheter shown in FIG. 31.

FIG. 33 is a side view of an embodiment of a nebulizing catheter incorporated into a suction catheter.

FIG. 34 is a detailed sectional view of the tip portion of the suction catheter - nebulizing catheter embodiment of FIG. 33.

FIG. 35 is a perspective view of the catheter of FIG. 33 positioned in an endotracheal tube in a patient's respiratory system.

FIG. 36 is cross sectional view of the embodiment of FIG. 33.

FIG. 37 is a perspective view similar to FIG. 35 showing the suction catheter advanced during an further stage of operation.

FIG. 38 is a side view of a proximal end of an endotracheal tube illustrating an arrangement of receiving a suction catheter and a nebulization catheter into the endotracheal tube.

FIG. 39 is an alternative to that shown in FIG. 38.

FIG. 40 is another alternative to that shown in FIG. 38.

FIG. 41 illustrates catheter in accordance with an example of the invention incorporating aerosol delivery by nebulization.

FIG. 42 shows another catheter in accordance with an example of the invention incorporating aerosol delivery by nebulization.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

[0016] The present invention facilitates the provision of controlled and efficient delivery of an aerosolized medication to the lungs of a patient by nebulization of a medication at a distal end of a catheter positioned in the respiratory tract. Throughout this specification and these claims, the nebulization catheter is described as used for the delivery of medicine or medication. It is intended that the terms "medication", "medicine", and "drug" should be understood to include other agents that can be delivered to the lungs for diagnostic or therapeutic purposes, such as tracers, or for humidification.

Nebulizing Catheter - Basic Configuration

[0017] FIGS. 1 and 2, show an endotracheal tube 10 which may be a conventional endotracheal tube. The endotracheal tube 10 may have an inflatable cuff 12 located close to its distal end to facilitate positioning the tube 10 in the patient's trachea, or alternatively the endotracheal tube 10 may be of a type without an inflatable cuff. The inflatable cuff 12 is connected via a separate inflation lumen in the endotracheal tube 10 to a proximal fitting 13 for connection to a source of inflating gas (not shown). The endotracheal tube 10 has a proximal end connected to a manifold fitting 14. The fitting 14 has a port 15 suitably adapted for connection to a ventilator

circuit (not shown). The fitting 14 also includes another port 16 that permits the introduction of a separate catheter into the endotracheal tube from the proximal end. The fitting 14 may be similar in construction to the elbow fitting described in U.S. Pat. No. 5,078,131 (Foley), the entire disclosure of which is incorporated herein by reference. In FIG. 1, a nebulizing catheter 20 which is described herein forfacilitating an understanding of the invention, is located in a position ready to be inserted into a ventilation lumen 22 of the endotracheal tube 10 via the proximal fitting 14. In FIG. 2, the nebulizing catheter 20 is positioned fully in the endotracheal tube 10 with a proximal end extending out of the port 16 of the proximal fitting 14.

[0018] At a proximal end of the nebulizing catheter 20 is a manifold 24. The manifold 24 includes at least a gas port 28 and a liquid (medicine) port 32. These ports 28 and 32 may include conventional attaching means, such as luer lock type fittings. In addition, these ports 28 and 32 may also include closure caps 31 that may be used to close the ports when not in use and may be popped open when connection to a gas source or a liquid source is desired. Optionally, the manifold 24 may also include a filter located in-line with either the gas port 28 or the liquid port 32 or both ports to prevent lumen blockages by particulate matter. The nebulization catheter 20 includes at least two separate lumens (as shown in FIG. 2A). A first lumen 33 is used for conveyance of a liquid medicine and communicates with the port 32 on the manifold 24. The other lumen 34 is used for conveyance of a pressurized gas and communicates with the port 28 on the manifold 24. The liquid lumen 33 communicates with a distal liquid orifice 35 and the gas lumen 34 communicates with a distal gas orifice 36 near a distal end 37 of the nebulization catheter 20. The distal opening 36 of the pressurized gas lumen 34 directs pressurized gas across the distal liquid lumen opening 35 thereby nebulizing the liquid medication so that it can be delivered to the patient's lungs. The distal liquid orifice 35 may be open or may be provided with a porous material plug or a sponge-like or felt-like material plug which may extend slightly from the distal orifice and that allows liquid to flow from the orifice yet reduces the likelihood of liquid drooling from the tip.

[0019] The length of the nebulization catheter 20 should be sufficient so that the distal end 37 can be located in the desired location in the respiratory system while the proximal end (i.e., including the manifold 24) is accessible to the physician or other medical personnel for connection to suitable gas and liquid supplies external of the patient's body. Accordingly, the length of the nebulization catheter is dependant upon the size of the patient in which it is being used. A shorter nebulization catheter may be preferred in smaller patients, such as infants or children, and a longer nebulization catheter may be needed for adults. For example, a nebulization catheter suitable for adults may have a length of approximately 45 cm. In one embodiment, approximately 30 cm of the nebulizing catheter 20 is in the endotracheal tube 10. The nebulization catheter may be introduced into the respiratory system through a patient's mouth or via a tracheostomy tube or through the nasal passages. The nebulization catheter may also be used to deliver an aerosol to a patient's nasal passages in which case the length may be correspondingly shorter.

[0020] As explained in more detail below, the generation of an aerosol plume with the desired geometry, particle size, velocity, etc., requires that the distal gas and liquid orifices have small dimensions. Also as explained below, the distal gas orifice 36 and the distal liquid orifice 35 should be in close proximity to each other in order to produce an aerosol with the desired characteristics and efficiency. Further, in order to provide the desired medicine delivery rates and to operate with reasonably available pressure sources, the liquid and gas lumens in the nebulizing catheter should be as large as possible, consistent with anatomical requirements. Accordingly, the nebulization catheter 20 has a multiple stage construction with a larger shaft size and larger lumens in a main shaft section and a smaller shaft size and smaller lumens in a distal shaft section.

[0021] As shown in FIG. 2A, the nebulizing catheter 20 is composed of a shaft 38 having a main section 39 and a distal section 40. In the main shaft section 39 of the nebulization catheter, the liquid and gas lumens 33 and 34 have a larger size than in the distal shaft section 40. For example, in the main shaft section 39, the liquid and gas lumens each may have an I.D. of approximately 0.254 to 0.760 mm (0.010 to 0.030 inches). At a most proximal end where the main shaft section 39 connects to the manifold 24, the lumens may be even larger. In the distal shaft section 40, the liquid and gas lumens taper to a much smaller I.D. with the liquid lumen approximately 0.051 to 0.203 mm (0.002 to .008 inches) or even smaller and the gas lumen 0.051 to 0.510 mm (0.002 to 0.020 inches). In a preferred embodiment, the liquid and gas orifices 35 and 36 are less than 3.175 mm (0.125 inches) apart, and more preferably less than 0.762 mm (0.030 inches) apart, and in a most preferred embodiment less than 0.025mm (0.001 inches) apart. In a nebulizing catheter having an overall length of 45 cm (17,72 inches), the main shaft section 39 may be approximately 25 cm (9.84 inches) and the distal shaft section 40 may be approximately 20 cm (7.87 inches). Also, although the liquid and gas lumens are shown to be side by side in FIG. 2A, they may also be constructed to have an coaxial or other arrangement. Further, although the main shaft section 39 is shown to be of a uniform diameter and profile, alternatively it may also have a tapered diameter and profile such that the entire shaft 38 is tapered along its length.

[0022] The nebulizing catheter 20 is removable, and replaceable with respect to the endotracheal tube 10. This provides several significant advantages. First, the nebulizing catheter 20 may be specifically adapted and chosen to have the desired operating characteristics

suitable for delivery of the particular medication being administered to the patient. In addition, the fact that the nebulizing tube 20 is removable and replaceable provides versatility and flexibility regarding the therapy and dosage regime that can be chosen by the physician. For example, a decision by the physician whether to deliver a medication to the respiratory tract, and the selection of the type and dosage of the medication to be delivered, need not be made by the physician until after the endotracheal tube is already in place in the patient. When the physician determines the proper type of medication to the delivered to the patient via the respiratory tract, the appropriate nebulization catheter can be selected and inserted into the endotracheal tube. Further, the nebulizing catheter 20 can be removed after it is used and therefore it is not necessary for the nebulization catheter to be left in the patient and occupy space in the patient's respiratory tract or in the endotracheal tube 10 when it is no longer needed. In addition, the decision regarding the proper type of medication can be revisited again at any time after the endotracheal tube is in place. If a different type of nebulizing catheter is required, such as for sterility purposes, the endotracheal tube need not be replaced as well.

[0023] Another advantage of providing the nebulization catheter as a separate, removable device is that it can be accommodated in a variety of other instruments and/or devices. For example, the nebulization catheter of FIGS. 1 - 5 is shown used in an endotracheal tube; however, the nebulization catheter could also be positioned inside of a bronchoscope, such as in a working channel of a bronchoscope. The nebulizing catheter could be positioned in any instrument that is positioned in the respiratory tract and that can accommodate the nebulizing catheter size.

[0024] The nebulizing catheter may be provided with radiopaque markings 41 to facilitate positioning and placement. The radiopaque markings 41 may be provided by radiopaque bands of metal or heat shrunk bands of doped radiopaque plastic that are attached to the nebulizing catheter, or alternatively the markings may be provided by doping the plastic material of the nebulizing catheter with a radiopaque material. Alternatively, a radiopaque dye may be added to the liquid being delivered by the nebulization catheter to assist observation. The markings 41 may be graduated to facilitate recognition, or alternatively may extend over a portion or all of the nebulizing catheter. In still a further embodiment, the markings may be formed of a ultrasonic reflectors, e.g. textured material, that are visible by means of ultrasonic imaging. The nebulization catheter may also include a stripe 43 extending along a side of the shaft (as shown in FIGS. 5 and 6). The stripe 43 may be radiopaque or ultrasonically visible and may be used to determine the rotational orientation of the shaft. The stripe may be formed by a coextrusion process or by embedding a wire in the wall of the nebulization catheter.

[0025] One method that may be employed to facilitate positioning of the nebulization catheter is to monitor the pressure at the distal end of the endotracheal tube as the nebulization catheter is being advanced. Monitoring the pressure at the end of the endotracheal tube may be accomplished through one of the endotracheal tube lumens. The gas source connected to the proximal end of the nebulization catheter may be operated so as to expel a gas from the distal end of the nebulization catheter as it is being advanced. The gas being expelled from the distal end of the nebulization catheter affects the pressure being detected through the endotracheal tube. When the distal end of the nebulization catheter passes the distal end of the endotracheal tube, the pressure being measured through the endotracheal tube abruptly changes thereby providing a clear indication of the location of the distal end of the nebulization catheter relative to the endotracheal tube.

[0026] The nebulizing catheter may also include a safety stop 44 located along a proximal portion that engages a portion of the endotracheal tube proximal portion or a fitting thereon, as shown in FIG. 2. The safety stop 44 ensures that the distal end of the nebulizing catheter 20 is correctly positioned with respect to the distal end 46 of the endotracheal tube 10 and prevents the distal end 37 of the nebulizing catheter from extending too far into the trachea. In addition to the safety stop 44, the proximal portion of the nebulizing catheter 20 may also have graduated markings 48 that would be visible to the physician handling the proximal end of the nebulizing catheter to enable a determination of the position of the distal end 37 of the nebulizing catheter 20 relative to a distal end 46 of the endotracheal tube 10.

[0027] The nebulizing catheter 20 may also include a critical orifice 49 located at a proximal portion of the nebulizing catheter. The critical orifice 49 may be formed by a small critical opening located in line with the gas pressurization lumen 34 of the nebulizing catheter shaft close to the manifold 24. The critical orifice 49 is sized so that if the nebulization catheter is supplied with a flow in excess of its designed operating flow, the critical orifice will allow only the designed operating flow to pass through to the distal gas orifice. Alternatively, a safety valve may be located in the proximal portion of the catheter shaft. The safety valve would be designed to open if supplied with an excess of pressure.

[0028] In addition, the nebulizing catheter may include a centering device 50. The centering device 50 is located close to a distal end of the nebulizing catheter shaft and helps to center and align the distal end of the nebulizing catheter for improved performance, as explained in more detail below.

[0029] The removable nebulization catheter 20 may be enclosed in a storage sheath 51. The storage sheath 51 may be similar to the type of storage sheaths used in conjunction with suction catheters. The storage sheath is preferably flexible, collapsible, or extendable to accommodate insertion of the catheter. The storage sheath 51 may be connected to the fitting 14. The stor-

age sheath 51 can be used to receive the nebulizing catheter 20 when it is being withdrawn from the endotracheal tube 10. The storage sheath 51 is sealed and can maintain the withdrawn nebulizing catheter in an isolated condition when it is temporarily removed from the patient's respiratory system. The storage sheath 51 also allows the physician to re-insert the nebulization catheter into the patient. In this manner, the nebulization catheter can be reused in a limited way with respect to a patient and can be maintained in a sterile condition while withdrawn from the patient. The storage sheath 51 may have a distal sleeve 53 that can slide along the shaft of the nebulization catheter so that the nebulization catheter may be advanced into the ventilation lumen of the endotracheal tube or withdrawn into the storage sheath 51. The sleeve 53 may have a close fitting seal 55 located therein which is designed to clean and/or wash the nebulization catheter when it is withdrawn into the sheath. Alternatively, a cleaning seal 55 may be located in the port 16 of manifold fitting 14.

[0030] Another feature that may be used in conjunction with certain procedures is radiation shielding. Some procedures for which the nebulization catheter may be used may involve the delivery of radioactive agents, e. g. tracers to the lungs. To minimize exposure to radioactive materials, the nebulizing catheter may be provided with shielding over all or a significant portion of the overall length of the catheter. Shielding may also be provided at the liquid source reservoir.

[0031] The nebulizing catheter is preferably constructed of a biocompatible, chemically resistant polymer in order that it is suitable for use with a wide variety of drugs. The catheter shaft is preferably clear to allow visualization of contaminants or blockages of the interior lumens. Also, the portion of the catheter shaft that forms the liquid lumen 33 is preferably composed of a relatively non-compliant material. In a present embodiment, the catheter shaft is composed of a polymer such as polyethylene or nylon. A polymer tubing is extruded with multiple lumens to be used for the separate gas and liquid lumens. In order to produce a nebulization catheter with the tapered distal section 40, a multi-lumen extruded tubing may be drawn down in a portion thereof to form the tapered distal section 40. The draw down ratio may be selected to provide a nebulization catheter shaft with the desired dimensions. The draw down process serves to make the lumens smaller in size distally as well as closer together while maintaining the proximal cross sectional profile of the multi-lumen tubing. The larger proximal profile provides for greater pushability in the catheter shaft and facilitates manufacturing by making the manifold connection easier. The draw down ratio used on the extruded polymer tubing may be on the order of 2-to-1, 5-to-1, or even as high as 20-to-1 or higher. Prior to drawing down, the extruded polymer tubing is preferably exposed to high energy radiation to crosslink the polymer molecules to provide for favorable material properties, such as the ability to maintain orifice dimensions and tolerances. The radiation may have an energy of approximately 10-700 kgy. After the crosslinking step, the tubing is heated to its transition temperature between its melt and glass states, and is drawn down by the desired ratio.

[0032] As an alternative to drawing down the extruded tubing, the multi-stage nebulization catheter shaft may be formed by a bubble extrusion process wherein the desired tapered distal section is formed directly in the shaft as it is being extruded. Again, this process may be used for manufacturing efficiency and convenience. As another alternative, the multi-stage shaft may be formed by a combination of both bubble extrusion and drawing down. Still another alternative for forming the desired tapered profile for the nebulizing catheter shaft is to use a material that can be cold drawn in order to cause a sharp neck down in diameter, such as a linear low density polyethylene. Although the process for forming the tubing is particularly suited for producing a nebulization catheter shaft for use in delivering medicine to the respiratory tract, it should be understood that the process could be used to produce aerosol nozzles for non-medical purposes as well.

[0033] Alternatively; all or part of the nebulization catheter shaft can be molded, especially at locations where close tolerances are preferred such as at the tip.

[0034] After the shaft is formed with the desired stages, it is cut and assembled with the other components of the nebulizing catheter. Although the nebulization catheter is preferably constructed of a polymer, in an alternative embodiment it could be formed of other materials such as a metal, especially a malleable metal to facilitate drawing, shaping or forming orifices. During the manufacturing process, the nebulizing catheter may be pre-sterilized by means of a conventional process, such as a gamma ray or electron beam. The nebulizing catheter is preferably disposable after use with a single patient, but may be reused to a limited extent with a single patient provided that contamination can be prevented such as through the use of the sheath 51, described above. The nebulizing catheter shaft preferably possesses torsional rigidity so that rotation of the proximal end is transmitted at a 1:1 ratio to the distal end. The nebulizing catheter may also be provided with an antiseptic coating.

[0035] Drug delivery rates are closely related to the particle size with larger particles providing greater delivery rates. The embodiments of the nebulization catheter described herein have the capability of generating particle distributions with a GSD between 2 and 2.5. Drug delivery rates in a range between approximately 5 and 1000 mg (.005 - 1.0 ml) per minute may be obtained. A variety of particle size distributions can be generated at most flow rates through selection of the catheter type and aerosol volume output. An aerosol of this type can be generated with the nebulization catheter using a gas flow rate as low as 0.1 liter/minute.

[0036] There are a number of factors that affect the

particle size generated. These factors include: (1) the gas orifice diameter, (2) the liquid orifice diameter, (3) the liquid delivery tube outer diameter and geometry, (4) the distance between the gas and liquid orifices, (5) the rate of gas delivery, and (6) the pressure of the liquid. Of course, the size of the solid particles in suspension, if present, in the liquid are a defining aspect of the aerosol particle size generated. In addition, there are other factors that affect the aerosol particle size such as the characteristics of the liquid, e.g. viscosity, suspension, surface tension and the composition of the driving gas, however, these factors affect the particle size of the aerosol generated to a lesser degree. By selectively varying these parameters, the size and size distribution of the aerosol particles can be changed from less than a micron to at least 10 microns.

[0037] The nebulization catheters described herein are suitable for delivery of an aerosol by nebulization with a volumetric particle size distribution comparable to other nebulization systems. Further, by generating an aerosol at a location in the trachea or even deeper in the bronchi, impaction losses in tract can be avoided. By reducing impaction losses, it may be acceptable to use larger particle sizes (e.g. greater than 5 microns). The combination of lower impaction losses and larger particle sizes may provide higher effective delivery rates than prior systems. Reducing impaction losses would enable an embodiment of the nebulization catheter to provide acceptable delivery rates with aerosol particle sizes greater than 5 microns.

[0038] Referring to FIGS. 3 - 5, there is provided an endotracheal tube 52 and a nebulizing catheter. The nebulizing catheter may be similar to the nebulizing catheter 20 shown in FIGS. 1 through 3. In FIGS. 3 - 5, the endotracheal tube 52 has an auxiliary lumen 56 in addition to its main ventilation lumen 60. Some endotracheal tubes provide auxiliary lumens through the shaft wall. The auxiliary lumen 56 is preferably sized and adapted to receive the separate nebulization catheter 20. This arrangement provides many of the same advantages as the arrangement of FIGS. 1 through 3. In addition, in this arrangement, the auxiliary lumen 56 may be provided with a distal aperture 64 that facilitates locating and aligning the distal end of 37 the nebulizing catheter 20 at a desired location for nebulization purposes.

[0039] In the arrangements shown in FIGS. 1-5, the nebulizing catheter 20 is shown used in conjunction with an endotracheal tube either of a conventional type 10, as in FIGS. 1 and 2, or of a type especially designed for use with the nebulizing catheter such as endotracheal tube 52 of FIGS. 3 - 5. The nebulizing catheter 20 may also be used without a separate endotracheal tube, i.e. the nebulizing catheter may be used on a patient who is not intubated, as shown in FIG. 6. If used on a spontaneously breathing patient (without an endotracheal tube), the patient should be properly anesthetized and/or that the airway passage of the patient be topically anesthetized. The nebulizing catheter 20 is positioned in the respiratory system of a patient directed past the carina 68 into one of the bronchi 72 of the lungs. Alternatively, the nebulizing catheter 20 may also be positioned proximal of the carina in the trachea, as desired. The nebulizing catheter may also be used on patients who have had tracheotomies or who have tracheotomy tubes.

[0040] In the arrangement of FIG. 6, a guiding sheath 73 is used. The guiding sheath 73 is used to help position the nebulizing catheter 20 in the respiratory system of the patient. The guiding sheath 73 includes a lumen through which the nebulization catheter 20 can be advanced into a desired bronchi site. To facilitate positioning the nebulization catheter, the guiding sheath 73 may have a pre-shaped distal end to facilitate locating the sheath in the desired airway passage. Alternatively, the guiding sheath 73 may have a distal end that can be formed into a desired shape by the physician just prior to insertion. The guiding sheath 73 differs from the endotracheal tube 10 of FIGS. 1-5 in that it may have a smaller outside diameter so that it can be advanced into smaller airway passages deep in the patient's bronchi past the carina 68. The inside diameter of the sheath 73 is large enough to advance the nebulization catheter. The guiding sheath 73 is particularly useful when the nebulization catheter 20 is being located deep in the patient's lungs, or when the nebulization catheter is used without an endotracheal tube. The guiding sheath 73 may also be used with an endotracheal tube through the ventilation lumen thereof. The guiding sheath is preferably composed of a torsionally rigid material so that the distal end of the guiding sheath is responsive to rotation at the proximal end.

Generation of Aerosol Plume

[0041] It has been discovered that the shape of the aerosol plume can be a significant factor affecting the rate and efficacy of the delivery of medication by an aerosol. In general, it is preferable to generate an aerosol that has a shape that minimizes particle impaction near the distal tip of the nebulizing catheter, given the location of the tip and the airflow conditions around it. For example, if the aerosol plume is wide, a portion of the drug may be wasted in the end of the endotracheal tube or on the wall of the trachea or other airway passage. On the other hand, if the plume is too narrow or the velocity too high, a portion of the drug may impact excessively on the patient's carina. In general, a low aerosol particle velocity is desirable. One of the reasons for this is to avoid impacting the carina with the discharge of high velocity aerosol particles. In addition, it is also generally desirable to have as wide an aerosol plume as possible while avoiding significant impact with the walls of either the endotracheal tube or the respiratory airway passage. The effects of aerosol plume velocity and geometry are related to anatomical factors. In some circum-

stances, e.g. away from the carina, a narrow, fast aerosol plume may be preferable to a slower, wider plume.

[0042] Regarding the embodiments described below, certain of the embodiments may be preferable from the standpoint of versatility, i.e. they may be able to deliver a variety of medications having different viscosities, suspensions, surface tensions, etc. Others of the embodiments may be more suitable for the delivery of specific types of medications or the delivery of particles of certain sizes.

[0043] Referring to FIG. 7, there is shown a tip configuration for a nebulizing catheter 132. The nebulizing catheter 132 may be either a stand alone-type of nebulizing catheter, or may be incorporated into an endotracheal tube either removably, as in FIGS. 1 - 5, or non-removably.

[0044] The tip 133 of the catheter 132 is formed with a plurality of lumens terminating in a plurality of orifices. An inner lumen 134 is used to convey the liquid medication and the surrounding lumens 135 convey the pressurized gas used to nebulize the liquid. This embodiment has the advantage that the orifice of the liquid lumen 134 is centered with a fixed spacing relative to the orifices of the gas lumens 135 around it. In the embodiment of FIG. 7, the multiple lumen construction may extend all the way back to the proximal end of the nebulizing catheter 132 or alternatively, only a distal segment may have the multiple gas lumen configuration in which case the pressurized gas may be conveyed through a single proximal lumen that connects to the multiple distal lumens.

[0045] FIGS. 8 and 9 show an alternative embodiment 136 of the multiple lumen nebulization catheter in FIG. 7. The embodiment in FIGS. 8 and 9 is useful when it is desired to provide the aerosol medicine with a pulsed delivery. The pulsed delivery may be timed to coincide with the inhalation of the patient so that aerosol is not wasted when the patient is exhaling. A potential drawback with pulsed delivery is that the aerosol may drool from the tip of the nebulizing catheter when the pressure being applied to the liquid is reduced to effect the pulsation. To avoid this potential problem, the nebulizing catheter 136 provides for closure of the liquid lumen when the pressure being applied to it is reduced. As in the previously described construction, the nebulization catheter 136 in FIGS. 8 and 9, has a centrally located lumen 137 for delivery of a liquid medicine and a plurality of lumens 138 surrounding the central lumen 137 for conveyance of a pressurized gas to nebulize the liquid at the distal orifice 139. In this arrangement the catheter 137 is formed of a low compliance material in the outer wall area 140 and a relatively high compliance material in the area 141 surrounding the centrally located liquid lumen 137. These differing compliance characteristics may be formed in the catheter shaft by coextruding a single tube with different materials. When using the embodiment of FIGS. 8 and 9, a constant, relatively high pressure is applied to the gas in the lumens 138. Liquid medicine is delivered via the lumen 137 and pressure pulses are applied to the liquid from an external delivery source, such as a pump. When the pressure in the liquid lumen 137 is low, the high pressure in the gas lumens 138 deform the compliant inner material 141 thereby compressing the liquid lumen 137 and closing it off, as shown in FIG. 8. When a pressure pulse is applied to the liquid in the lumen 137, it overcomes the compressive forces from the gas lumens 138 allowing the lumen 137 to open and permitting the liquid medicine to be delivered to the distal orifice 139 to be nebulized, as shown in FIG. 9. In this manner, the embodiment of FIGS. 8 and 9 provides for pulsed liquid nebulization with reduced possibility of drooling.

[0046] Another feature shown in FIGS. 8 and 9 is a porous plug located in the liquid orifice 139. This porous plug may be made of a felt-like material and may assist in the production of fine aerosol particles.

[0047] The embodiment of FIG. 10 shows a distal tip of another embodiment of the nebulizing catheter. In this embodiment, a nebulizing catheter 148 includes. a main shaft section 152 and a distal shaft section 156. The distal shaft section 156 is tapered to a tip 160. At the tip 160, a liquid orifice 164 is surrounded by a plurality of gas orifices 168. In a preferred embodiment, there are six gas lumens terminating in the six orifices 168. In this embodiment, the liquid orifice 164 has a diameter of approximately .002 inches and the gas orifices 168 each have a diameter of approximately .002 inches. This embodiment is similar to the embodiment of FIG. 7 except that the distal section 156 provides for a reduction in the tip size and corresponding modification of the nebulization plume properties. This reduction is preferable as it provides a smaller orifice size.

[0048] The embodiment of FIG. 11 shows a distal portion of a nebulizing catheter 172. In this embodiment, the nebulizing catheter includes a proximal shaft section 176 and a distal shaft section 180. The proximal shaft section 176 includes a plurality of lumens 184. A central one 188 of the plurality of lumens 184 is used to convey liquid medicine and the remainder of the lumens surrounding it are used to convey gas. The distal shaft section 180 connects to the distal end of the proximal shaft section 176 and defines a tapered cavity 192 between the distal end of the proximal shaft section 176 and a distal orifice 196. At least one of the plurality of lumens 184 is used to convey a pressurized gas that is discharged into the cavity 192. A tubular extension 200 extends the liquid lumen through the cavity 192 and distally out the orifice 196. The orifice 196 is sized to provide an annular region around the tubular extension 200 to permit the pressurized gas to flow through to nebulize the liquid medication that exits a distal orifice 204 of the tubular extension 200. In a preferred embodiment, the distal shaft section 180 is composed of stainless steel and the orifice has an I.D. of 0.635 mm (0.025 inches). The tubular extension 200 has an O.D. of 0.305 mm (0.012 inches) and an I.D. of 0.178 mm (0.007 inches). This

embodiment has the advantage of combining a relatively small distal profile with a relatively large proximal flow channel. Another advantage of this embodiment it that it provides for a balanced airflow around the liquid orifice 204.

[0049] FIG. 12 shows yet another tip for a nebulizing catheter. In FIG. 12, a nebulizing catheter 208 is shown for convenience having a coaxial configuration although it could also have a configuration similar to that of FIGS. 7, 10, or 11. In FIG. 12, a thin solid wire or filament 212 is located at a distal end of a liquid orifice 216 located at a distal end of an inner tubular member 220. The tapered wire 212 extends a short distance distally from the distal end of the inner tubular member 220. The tapered wire 212 is located with respect to the liquid orifice 212 so that liquid being conveyed through the inner member 220 continues to flow distally of the distal orifice 216 along the wire 212, i.e. adhering to it by surface tension. Of course, once the liquid reaches a distal tip 224 of the wire 212, it is entrained and nebulized by the gas flow from the annular region 228 defined between the inner tubular member 220 and an outer tubular member 232. As mentioned above, one of the factors that affects the nebulization plume particle size and geometry is the size of the distal liquid orifice. In general, a smaller liquid orifice produces smaller particles and a narrow aerosol plume cone. In the embodiment of FIG. 12, the thin wire 212 carries only a small amount of liquid along it so that it functions similarly to an orifice of a very small size. Accordingly, the embodiment of FIG. 12 has the potential for producing an aerosol of very fine particles. In the embodiment of FIG. 12, the outer tubular member has an I.D. of approximately 0.508 mm (0.020 inches). The inner tubular member has an I.D. of approximately 0.152 mm (0.006 inches). The thin wire has an O.D. of approximately 0.051 mm (0.002 inches). The wire or filament 212 may be composed of a metal wire or a polymer wire, such as a polyolefin fiber like Spectra fiber. Alternatively, the filament 212 may be composed of a porous or felt-like material, such as nylon or Porex, in which case it may be wider in diameter than if made of a solid material.

[0050] FIG. 13 shows an alternative catheter in which there is a distal end of a nebulizing catheter 236 having a tapered wire or filament 240 located at the distal end of a lumen of an inner tubular member 244. The tapered wire 240 in this embodiment has a curved shape that is designed to whip in a spiral when it is in a flow of air. In the catheterof FIG. 13, when pressurized gas flows through the annular region 248, it causes the tapered wire 240 to whip around with a spiral motion. The length of the wire 240 is chosen so that it does not impact the wall of the trachea or other airway passage when it moves in a spiral whipping motion. In one embodiment, the wire 240 has a length of approximately 1 - 2 mm. The tapered wire 240 carries the liquid out to its tip for entrainment, and the nebulization plume is formed with a conical shape. The width of the plume may be changed by changing the length of the filament 240. The speed of the spiral motion can be controlled by appropriate selection of wire stiffness and air foil shape. In general, the spiral plume produced by the catheter of FIG. 13 will be wider than that of the catheter of FIG. 12 and have less forward velocity. Both these characteristics may be favored in a nebulization catheter.

[0051] FIG. 14 shows an alternative nebulization catheter 340 having an additional lumen 365. This additional lumen 365 may have an I.D. of approximately 0.508 mm (0.020 inches). This additional lumen 365 may be used for an optical fiber viewing scope 366 for illumination and visualization of the distal end of the nebulization catheter 340. The optical viewing scope 366 may be permanently installed in the catheter 340 or preferably may be removable. A distal end 367 of the lumen 365 is open or covered with a transparent lens so that the area distal of the catheter 340 can be observed via an optical viewing device connected to a proximal end of the optical fiber 366. This enables a physician to observe the alignment of the distal end of the nebulization catheter and also observe the nebulization when it occurs. The gas orifice 356 may be located so that the pressurized gas that is expelled helps to keep the distal end of the viewing lumen 365 clear. An optical fiber viewing channel may be incorporated into any of the nebulization catheters disclosed herein. When the additional lumen 365 is occupied by a removable viewing scope, it may be used for other purposes such as pressure sensing, gas sampling, over pressure relief, or other diagnostic or therapeutic purposes. Alternatively, another lumen may be provided for these purposes.

[0052] The catheter of FIG. 14 also shows opposing orifices. A tubular extension 360 extends distally of the end of the catheter shaft and is oriented at an angle, e.g. 90 degrees, to the direction of the axis if the catheter shaft. The tubular extension 360 opens to a distal liquid orifice 364 from which the liquid being conveyed in the lumen 352 exits. In this embodiment, a second tubular extension 363 communicates with the gas lumen 348 and opens to a distal gas orifice 367. The second tubular extension 363 is also oriented relative to the axis of the catheter shaft, e.g. by 90 degrees, so that is aimed toward the distal liquid orifice 364 in order to nebulize the liquid exiting from the liquid orifice 367.

Alignment of the Aerosol Plume

[0053] It is further recognized that another factor that contributes to the efficiency of the nebulization is the position of the nebulization catheter relative to the anatomical environment. For example, even if the nebulization catheter being used develops an optimal plume, the delivery efficiency of the catheter may be significantly impaired if the plume is directed into the wall of the endotracheal tube, the trachea or other airway passage. Accordingly, proper location, orientation, and alignment of the nebulization catheter in the anatomy can be an important factor contributing the delivery of medicine via

a nebulization catheter. In general, it is preferable to align the catheter coaxially in the airway passage in which it is located.

[0054] It is also noted that an endotracheal tube, if present, can adversely effect delivery of aerosol from a separate nebulization catheter. For example, an endotracheal tube has an inner diameter that is smaller than the diameter of the trachea so that if the nebulization takes place inside the endotracheal tube, a portion of the aerosol may impact the inner wall of the endotracheal tube and thereby be wasted. Most conventional endotracheal tubes have a curved distal end that is relatively rigid so that when it is in place in the trachea of a patient, the distal end of the endotracheal tube is oriented off center. This can affect the orientation of a nebulization catheter located in the endotracheal tube causing it direct its aerosol into the trachea wall even if the nebulization catheter is positioned so that its distal end is located distally of the endotracheal tube. In general, it is desirable to allow the aerosol particles to avoid impaction for several centimeters after the aerosol is produced so that the aerosol particles can lose their velocity and become entrained in the inspiratory airflow.

[0055] The catheter in FIG. 15 is directed at providing improved alignment of a nebulization catheter in a patient's trachea. In FIG. 15, an endotracheal tube 700 is positioned in a trachea 704 of a patient. The endotracheal tube 700 is of a type that has an inflatable cuff 708 located around a distal exterior side to facilitate positioning and alignment of the endotracheal tube 700 in the trachea 698. Extending through and out of a distal end of the endotracheal tube 700 is a nebulization catheter 712. The nebulization catheter 712 may be similar to any of the embodiments of the nebulization catheter described above. Located around a distal portion 716 of the nebulization catheter 712 is a spring centering apparatus 720. The spring centering apparatus 720 includes a retainer ring 724 fixed to the shaft of the nebulization catheter 712 and a plurality of arms 728 connected to the ring 724. In one embodiment, there are three arms 726. The arms 726 are flexible and resilient. The arms 726 may be made of a spring tempered metal or a suitable plastic. Located at the end of each of the arms 726 opposite its connection to the ring 724 is a ball 727. The spring centering apparatus 720 is deployed by first positioning the nebulizing catheter 712 including the spring centering apparatus in the lumen 728 of the endotracheal tube 700. The arms 726 are formed so that they assume a size larger than the diameter of the trachea or airway passage. Accordingly, when the centering device is positioned in the endotracheal tube 700, the arms are resiliently deformed into a compressed configuration with the balls 727 close to the shaft of the nebulizing catheter 712. To deploy the centering device, the nebulizing catheter 712 is advanced out the distal end of the endotracheal tube 700. When the balls 727 are advanced out the endotracheal tube 700, they spring out to an expanded size and engage the walls of the trachea or other airway passage. The balls 727 provide a relatively smooth surface to limit irritation or injury to the trachea walls or other airway passage. With the arms expanded, the nebulizing catheter is centered in the trachea or other airway passage so that a plume discharged from a distal end of the nebulizing catheter has minimal contact with the walls of the trachea or other airway passage. When it is necessary to remove the nebulizing catheter 712, it can be withdrawn in a proximal direction back into the endotracheal tube 700. In a preferred embodiment, the arms are formed of a thin resilient wire or polymer, preferably less than approximately 0.381 mm (0.015 inches) in diameter. The arms and/or the balls may be made of, or coated with, a radiopaque material. It is an advantage of the centering device shown in FIG. 15 that it is located somewhat in advance of the distal end of the nebulization catheter. This positions the arms 726 of the centering device in the portion of the trachea or other airway passage into which the aerosol will be initially flowing. Thus, the centering device orients the distal tip of the nebulization catheter relative to the portion of the trachea or other airway passage beyond the distal tip thereby helping to reduce impaction along this portion.

[0056] FIG. 16 shows an alternative nebulization catheter 729 which is used with an endotracheal tube as described above. The nebulization catheter 729 includes a centering device 730. The centering device 730 includes a plurality of arms 731 that are formed to resiliently extend outward from the axis of the catheter shaft to engage the wall of the patient's trachea or airway passage or the interior of an endotracheal tube depending upon the desired location of the distal end of the nebulization catheter. At the ends of each of the arms 731 are balls 732. The proximal ends of the arms 731 are formed of wires 733 that extend through lumens 734 in the shaft of the catheter 729. Each of the lumens 734 has a distal opening 735 from which an arm can extend. The distal openings are approximately 0.10 - 1.0 cm (0.004 to 0.039 inches) from the distal end of the catheter shaft. The proximal ends of the wires 733 exit the lumens 734 of the nebulization catheter via openings 736 that are close to the proximal end of the catheter in a portion of the catheter that would normally be outside the patient's body during use. Thus, the proximal ends of the wires 733 are accessible to the physician during use. By pulling and pushing on the proximal ends of the wires 733, the portion of the arms 731 that extend from the openings 735 can be adjusted. Thus, the arms 731 can be adjusted from a fully retracted to a fully advanced position by pulling or pushing on the proximal ends of the wires 733. In addition, since the proximal ends can of the wires 733 be adjusted in any intermediate position between the fully retracted and fully advanced positions, the physician can adjust the size of the centering device 730 to any appropriate size, as desired. Because the wires 733 should assume a desired shape when advanced out of the lumens in which they are contained

during positioning, it is preferable that they be formed of a material that has shape memory properties so that the desired expanded shape can be imparted to the wires during manufacture. In one embodiment, the wires may be formed of nitinol.

[0057] A second centering device 737 may also be provided. The second centering device 737 is located on the shaft of the nebulization catheter 729 proximally from the first centering device 730. The second centering device 737 may be formed of resilient wings formed of a material such as plastic or metal that extend radially outward from the shaft. The second (or proximal) centering device 737 helps keep the distal portion of the catheter 729 in alignment.

[0058] FIG. 17 shows another alternative nebulizing catheter 738 which may be similar to the catheter 20 of FIG. 1. The nebulizing catheter 738 includes a centering device 739. The centering device 739 includes a wire loop 740 located at a distal end of the catheter. One end 741 of the loop 740 connects to the distal end of the nebulizing catheter shaft. The other end 742 of the wire loop 740 enters an opening 743 in the shaft that communicates with a lumen 744 that extends to a proximal end of the catheter 738. A proximal end 745 of the wire exits the lumen 744 via an opening 746 in a proximal portion of the nebulizing catheter which is normally outside the patient's body during use. The size of the wire loop 740 can be adjusted by advancing or withdrawing the proximal end 745 of the wire. In this arrangement it can be determined that the centering device is fully retracted when the wire 745 cannot be withdrawn any further. The position of the distal end of the nebulization catheter can also be determined by the resistance to further retraction caused when the loops or arms engage the distal end of the endotracheal tube. When in an expanded size, the wire loop 740 engages the walls of the trachea or airway passage or the interior of the endotracheal tube depending upon where the distal end of the nebulizing catheter is positioned. The size of the wire loop 740 can be adjusted from a fully reduced size to a fully expanded size as well as intermediate sizes.

With the embodiment of FIG. 17, the size of the loop can be adjusted to different size airway passages in different patients or alternatively the size of the loops can be adjusted to different airway passages in the same patient if the physician desires relocating the nebulizing catheter to different locations in a patient's respiratory tract. More than one wire loop may be provided at the distal end of the nebulizing catheter. It is noted that the wire loop 740 may also be used in for facilitating positioning over a guide.

[0059] FIGS. 18 and 19 show another alternative nebulizing catheter 747 having a shaft portion 748 and a wire loop 749 extending from a distal end of the shaft 748. In this embodiment, the wire loop 749 is connected at each end 750 and 751 to the distal end of the catheter shaft 748. A retractable sheath 752 is positioned over the nebulizing catheter shaft 748. The sheath 752 can be advanced and withdrawn relative to the catheter shaft 748. When it is desired to maneuver the nebulizing catheter into a desired position in the respiratory tract of a patient, the sheath 752 is advanced over the loop 749 to maintain a low profile, as shown in FIG. 19. When the distal end of the nebulizing catheter is suitably positioned, the sheath 752 is then retracted, as shown in FIG. 18, allowing the loop 749 to expand to its expanded size to center and align the distal end of the nebulizing catheter in the respiratory tract. The loop 749 may be formed of a superelastic material such as nitinol.

[0060] As noted above, proper positioning and alignment of the nebulization catheter can be an important factor affecting drug delivery efficiency. In general, it is preferable to position the tip of the nebulizing catheter as closely to the central region of the trachea (or other respiratory passage, such as the bronchi) as possible. It is further noted that even if the catheter can be centered relative to the trachea, if a section proximal to a centering device is misaligned, it can affect the directional orientation of the tip. This situation is represented in FIG. 20 in which a nebulizing catheter 753 is centered, but the tip is not properly aimed to provide an optimum plume. This potential problem can be overcome by using a nebulizing catheter 754 as shown in FIG. 21 located in a trachea 755 of a patient. The nebulizing catheter 754 extends out the end of an endotracheal tube 756. A first centering apparatus 757 is located on a main shaft 760 of the nebulizing catheter 754 close to the distal end 764. The first centering device 757 may be similar to the centering devices shown in FIGS. 15 - 19. A second centering device 768 is located axially along the nebulizing catheter shaft 760 proximally from the first centering device 757. The second centering device 768 may be the same as the first centering device 757. As shown in FIG. 21, the two centering devices 757 and 768 not only serve to position the nebulization catheter 754 centrally in the trachea, but also serve to align the nebulizing catheter tip to expel the plume along a central axis of the trachea.

[0061] The proximal centering device 768 may be substituted by another type of centering device or may employ the endotracheal tube 756 for this purpose, as shown in FIG. 23. If the endotracheal tube is used to assist in centering the nebulization catheter, it may incorporate a distal, elongated occlusion cuff 772 or balloon to coaxially align it accurately in the trachea. Most conventional endotracheal tubes are provided with a curvature to facilitate positioning the trachea of a patient. In addition, most conventional endotracheal tubes are relatively stiff. These factors may result in the misalignment of the distal end of the endotracheal tube relative to a patient's trachea as illustrated in FIGS. 20 and 21. In order to use the endotracheal tube for centering of the nebulization catheter, it is preferable to make the tip of the endotracheal tube straighter and/or more flexible than in conventional endotracheal tubes to ensure proper concentricity with the occlusion balloon and the

trachea. An endotracheal tube with a straighter and more flexible tip is shown in FIG. 22. In addition, the endotracheal tube may be provided with a centering or aiming device 776 for aligning the nebulization catheter 764. In the embodiment of FIG. 22, the aiming device 776 is formed by a plurality of flexible or resilient wings the extend from the wall of the endotracheal tube 756 toward an axially central position.

[0062] Appropriate centering and aiming of the nebulization catheter can be affected by anatomical factors. It is noted that in some circumstances, it is preferable to position the distal tip of the nebulization catheter into either bronchus of the lungs or even into separate bronchia. Positioning of the nebulizing tip closer to the alveoli may enhance drug delivery efficiency. In a situation in which it is desired to place the nebulizer tip in both bronchi of the lungs, a nebulizing catheter 780 with dual tips can be employed, as shown in FIG. 23. When using a dual tip catheter such as shown in FIG. 23, centering and aiming can be important considerations because of the narrower air passages in each of the bronchi. To provide for centering and aiming of a dual tip nebulizing catheter, each of the tips 784 and 788 may be provided with its own centering apparatus, such as 792 and 796. These centering devices may be similar to the centering devices described above. Alternatively, the centering devices 792 and 796 may be formed of arms or struts, made of a flexible or resilient material, that bow out from the shafts of each of the tips 784 and 788, as shown. These struts may be formed with a shorter length in order to fit into smaller airway passages or alternatively they may be made to provide a range of deployment sizes to accommodate different airway passages.

[0063] As an alternative to providing a nebulizing catheter with dual tips 784 and 788 as shown in FIG. 23, if delivery of aerosolized medicine into separate branches of the lungs is desired, it may be preferred to use a nebulizing catheter with a single nozzle tip that has multiple orifices or jets aimed toward the desired branches.

[0064] With respect to all the centering devices described above, it is noted that some aerosol may impact the wires or loops that form the centering devices and accordingly, the centering devices are preferably constructed of wires or other materials having a small diameter or cross section to minimize losses due to such impaction. Moreover, the overall improved efficiency due to the reduction in aerosol impaction on the walls of the trachea or other airway passage is expected to more than compensate for amy losses due to impaction on the centering device.

[0065] Another alternative means for centering the distal end of a nebulization catheter in the air passage is to use part of the pressurized gas for a pneumatic centering device. Air jets generated from two or more outward directed orifices spaced evenly around the outer circumference of the nebulizing catheter near the tip can be used to center the catheter in the airway. This alternative may help avoid irritation and provide additional advantages compared to physical centering devices.

[0066] Another alternative way to help center the nebulizing catheter in the patient's airway passage is to use a balloon or wire centering device placed near the nebulizing catheter tip. The balloon or wire centering device can be temporarily inflated to double check the placement of the nebulizing catheter tip in relation to the endotracheal tube tip. To use this feature the nebulizing catheter is advanced beyond the endotracheal tube tip using markings on the proximal shaft to judge the distance. The centering device or balloon would then be expanded to a diameter larger than the endotracheal tube and the catheter retracted until the centering device or balloon could be felt engaging with the endotracheal tube tip or until the endotracheal airflow was obstructed.

Operation and Flow Control

[0067] As mentioned above, the driving gas used to pressurize the gas lumen may be pure (e.g. 100%) oxygen at a pressure of 241.32 - 344.74 kPa (35-50 psi). Other gases and pressures may be used with suitable adjustments to provide for the desired particle size. The pressurized gas also may be humidified by a bubbler or other suitable means and warmed, if necessary.

[0068] Regarding the liquid lumen, one way to deliver the liquid drug through the nebulizing catheter is by a manually operated syringe. To delivery a liquid drug in this manner, a syringe containing the liquid medicine to be nebulized is connected to the liquid port on the manifold connected to a proximal end of the nebulizing catheter. Then, the liquid is injected while the pressuring gas is being supplied to the nebulizing catheter via the gas inlet port on the nebulizing catheter manifold. Using a manually operated syringe is reliable, easy to use, and may be preferred when it is desired to deliver only a small amount of medication.

[0069] In a preferred embodiment, the liquid drug is delivered to the nebulizing catheter from a pressurized source. A pressurized source for the liquid medicine can provide for a generally higher and more uniform pressure. A high pressure assists in clearing any blockages that may occlude the liquid lumen. Pressurization of the liquid lumen also can ensure that all the liquid drug is evacuated from the catheter tip. In addition, use of a liquid pressurization source can provide for drug delivery for a longer period of time or a drug delivery that is timed or pulsed to coincide with operation of a ventilator, if used. In a preferred embodiment, the same pressure source (at 344.74 kPa (50 psi)) that is used to provide the gas pressurization can also be used to provide for pressurization of the liquid. Some ventilators have an auxiliary port that are used for externally located nebulizers. The pressure flow from this auxiliary port may be used as a pressure source to drive the liquid and gas supplies of the embodiments of the nebulizing catheter considered herein. Alternatively, a sensor located in the

flow from this auxiliary port may be used to trigger another control device that operates the pressurized liquid and gas supplies.

[0070] In a preferred embodiment, the generation of the aerosol can be synchronized with the inhalation of the patient. In one embodiment, this can be accomplished with a manually operable control gas valve on the gas pressure line to the liquid input port. This may be suitable when the medicine can be delivered in a short period of time, e.g. a few respiratory cycles. Alternatively, when it is preferred to deliver the medicine for an extended period of time, it may be preferred to employ a system that can automatically deliver medicine via the nebulizer from a source of liquid medicine. In such a system, the gas and/or liquid flow are triggered by the patient's respiratory cycle with the use of an electronic pressure sensor and relay actuator.

[0071] An important factor relating to effective delivery of medication via a nebulizing catheter is the flow control system for pressurizing and supplying the gas and liquid to the proximal end of the nebulization catheter. In many circumstances, it is envisioned that medication will be delivered to the patient via a nebulization catheter that is in place in the patient over an extended period of time, such as several hours or days. In such circumstances, it would be preferred to use a system that automatically delivers the proper dosage of medication from a supply of the medicine to the patient at the proper rate, and further that can operate automatically and unattended. Further, it would be preferred to provide a means to detect when the supply is running low so that either the nebulization catheter can be disconnected or a new supply provided. FIGS. 24 and 24 show several embodiments of a reservoir and pressurization system for use with a nebulizing catheter.

[0072] Referring to FIG. 24, a reservoir and pressurization assembly 800 is connected to a proximal end of a nebulization catheter. The nebulization catheter may be similar to any of the embodiments described above. The assembly 800 has a gas inlet port 804 that can connect to an external pressurized gas supply. The external pressurized gas supply may be the main gas supply of the hospital or may be provided by another unit. The external gas supply may provide oxygen at 344.74 kPa (50 psi). The gas inlet port 804 communicates with an airflow passageway 808 defined by and extending through the assembly 800. The assembly 800 includes a gas output port 812 that communicates with the fluid flow passageway 808 and which connects to a gas inlet port of the nebulization catheter (not shown). The gas output port 812 is located immediately downstream of the gas inlet port 804. Located in the fluid flow passageway 808 downstream of the gas outlet port 812 is a filter 816. The filter 816 is preferably a hydrophobic filter that allows the passage of gas but which would prevent the backflow of any liquid. Located downstream of the filter 816 in the fluid flow passageway 808 is an injection port and reservoir 820. This port 820 communicates with a supply of the liquid fluid medication to be supplied to the nebulizing catheter. Located next in the fluid flow passageway 808 is a capillary tube drug reservoir 824. The capillary tube reservoir 824 is comprised of a length of plastic tubing adapted to hold a supply of the liquid medication to be delivered. In the embodiment shown, the capillary tube reservoir consists of a helical coil of transparent tubing. Located downstream of the capillary tubing reservoir 824 is a liquid outlet 828 that connects to a liquid inlet port of the nebulization catheter (not shown). With the embodiment shown in FIG. 24, the transparent capillary tubing 824 provides a convenient and reliable way to ascertain the supply of medication to the nebulizing catheter. The capillary tubing because of its length is capable of containing a suitable supply of the medication. When the attending medical personnel observe that the medication is about to run out, a new supply can be readily provided. The clear capillary tube allows easy visualization of the drug flow by watching the gas-drug meniscus travel down the tube. Instead of relying on direct observation by medical personnel, the capillary tubing may be used with an automatic detection device, e.g. a photocell, that provides an alarm to the medical personnel upon detection that the medication is running out in the capillary tubing or that the meniscus has ceased moving due to a blockage. A blockage may also be detected by detection of an increase in pressure.

[0073] FIGS. 25 and 26 show another embodiment of a fluid reservoir and pressurization assembly 832. This embodiment includes a gas inlet 836, a fluid flow passageway 840, a liquid medicine supply vent 844, a filter 848, a capillary channel section 852, and an outlet port 856. In this embodiment, the filter 848 is located downstream of the filling vent 844. The filter 848 allows the pressurized gas to push the liquid drug during use but prevents the liquid drug from backing up to the vent during filling. In this embodiment, a second injection port 860 is provided downstream of the capillary section 852 and a second filter 864 is located downstream of the second injection port 860. The second filter 864 is preferably a filter having approximately a 20 µm retention. Also, in this embodiment, the capillary section 852 may be composed of a planar section 865. The planar section 865 may be a piece of plastic having a winding channel molded, routed or otherwise formed therein. The planar section 868 is preferably colored to provide suitable contrast with the liquid solution flowing therethrough. A transparent flat plastic cover is positioned over the winding channel of the planar section 865 to form the closed channel of the capillary section. The fluid channel in the capillary section preferably has an I.D. of approximately 2 mm (0.079 inches). The second inlet port 864 provides an additional means to add medication to the nebulizing catheter liquid flow. When the capillary channel in the section 852 has been filled, the gas is used to pressurize the tube and force the fluid to the catheter tip. The second filter 864 acts as a restrictive orifice to precisely meter the flow to the nebulizing catheter. The clear capillary

channel allows easy visualization of the drug flow by watching the gas-drug meniscus travel down the tube. The narrow tube makes the flow appear to move quickly even at slow delivery rates. Thus, any flow interruption can be easily observed. The capillary tubing section also ensures that almost 100% of the drug is delivered to the catheter tip since there is no dead space in the line except at the injection port 860.

[0074] During ventilation of a patient with an endotracheal tube, especially when intubation that takes place for a long period of time, it is considered desirable to humidify the air being delivered. When a nebulization catheter is used for delivery of medicine, either in conjunction with an endotracheal tube or even without an endotracheal tube, it is possible to utilize the nebulization catheter for providing humidification in addition to medicine delivery. An embodiment of a flow delivery system for a nebulizing catheter incorporating humidification is shown in FIG. 27. A suitably large reservoir 866 holds sterile water or saline. The reservoir 866 is connected to the liquid supply lumen 867 of a nebulization catheter 868. Solution is drawn into the nebulization catheter 868 from the reservoir 866 by negative pressure at the catheter tip, gravity, a pump in the solution supply line distal of the reservoir, or by pressurizing the reservoir by a suitable means.

[0075] Medicine may be added to the humidification water in at the following ways. In a first alternative, the medicine is added to the isotonic saline in the solution reservoir 866 thereby providing for high dilution and slow, continuous delivery of the medicine along with the water. In second alternative, the medicine is introduced into the solution supply line 867 via an injection port 869 between the reservoir 866 and the liquid lumen of the catheter 868. The medicine may be delivered to the injection port of the solution supply line from a solution reservoir system such as system 800 of FIG. 24. Using this latter alternative, a more concentrated dose of the medicine can be delivered at the specific time preferred by the physician. It may also be preferable to include a molecular sieve, check valve or air trap 870 between the reservoir 866 and the injection port to the to ensure that the medicine cannot flow or diffuse backwards into the reservoir 866.

[0076] When delivering medicine to the lungs or when delivering water for humidification, it may be desired to heat the liquid prior to delivery. This may especially be appropriate since expanding gases which are associated with the nebulization of liquids may remove heat from the body. In order to address this concern, a heating element 871 may be associated with the liquid supply line 867 to the nebulizing catheter 868. This heating element 871 may include an electric coil wound around the supply line 867 or may use a heated water flow in a tubing wound around the supply line 867. The heating element 871 may be used in embodiments that provide for humidification as well as those that do not. Alternatively, the heating element 871 may be associated with the gas supply line or with the liquid reservoir 866.

[0077] It is generally considered preferable to operate the nebulizing catheter so as to generate an aerosol that is carried by a patient's inhalation to the lungs. This requires a pulsing of the aerosol generation so that it is timed to coincide with the inhalation of the patient. If the patient is intubated, the timing of the nebulization can be synchronized with the operation of the ventilator. It is recognized that it may be preferable to begin the nebulization slightly in advance of, at, or slightly after, the beginning of the inhalation period in order to account for the distance between the nebulization tip and the alveoli. Also, it may be preferable to stop the nebulization slightly before the end of the inhalation period in order to avoid wasting aerosol after the inhalation flow has stopped.

[0078] This continuous pulsing of the aerosol can be accomplished by a system 872 as shown in FIGS. 28 and 29. FIGS. 28 and 29 show a portion of the flow control system for a nebulizing catheter. A flow line 876 has an inlet 880 and an outlet 884. The flow line 876 may be formed of a soft (e.g. compliant) tube. The inlet 880 connects to the source of liquid medicine and in particular may attach to the liquid outlet (828 or 856) of the liquid reservoirs shown in FIGS. 24 - 26. The flow line outlet 884 in FIGS. 28 and 29 connects to the liquid inlet port on the manifold of the nebulizing catheter, such as port 32 in FIGS. 1 and 2. Located around a portion of the flow line 876 is an actuator piston 888. The actuator piston 888 includes a solenoid pinch valve 892 that can impinge upon the portion of the liquid flow line 876 extending therethrough thereby pinching it off. The actuator piston 888 is connected to and operated by a controller that receives input from the ventilator (such as from the auxiliary port used for an external nebulizer) so that the actuator piston 888 is operated to open and close the flow line synchronous with the inhalation and exhalation phases of the ventilator. Instead of a solenoid piston, a metering valve or reversible syringe pump may be used.

[0079] In a preferred embodiment, the flow control system 872 uses a. dual solenoid arrangement to provide a draw-back feature. Pulsing of the liquid flow by actuation of the actuator piston 888 may result in some liquid being left at the distal nebulizer liquid orifice when the pressure is turned off. This may result in small amounts of liquid drooling from the distal liquid orifice tip since the liquid is not being expelled under controlled pressure conditions. In order to limit the occurrence of such drooling, a draw back feature is provided in the flow control system. The draw back feature is provided by a second solenoid 896 which is associated with a bladder 900 that communicates with the flow line 876. The bladder 900 communicates with the flow control line 876 downstream of the actuator piston 888. A small amount of fluid (liquid/air) occupies the bladder 900. The bladder is composed of an elastic material that is formed with a tendency to recover to an expanded size. When the ac-

tuator piston 888 opens to allow the flow of fluid to the distal end of the nebulizing catheter, the second solenoid 896 moves to a closed position thereby compressing the bladder 900 and squeezing fluid out of it into the fluid flow line 876, as shown in FIG. 28. During the exhalation stage of the ventilation cycle, the actuator piston 888 closes to shut off the flow of fluid to the distal end of the nebulizing catheter. When the actuator piston 888 closes, the second solenoid 896 opens, as shown in FIG. 29. This allows the bladder 900 to resiliently recover to its expanded size, and when it does, it draws fluid into it from the fluid flow line 876. Because the fluid flow line 876 is closed proximally at the actuator piston 888, when the bladder draws fluid into it from the fluid flow line 876, it draws fluid from the distal end of the fluid flow line that connects to the nebulizing catheter liquid lumen. This causes the entire column of liquid in the liquid lumen of the nebulizing catheter to move slightly in a reverse direction (i.e. proximally) thereby moving the liquid away from the distal orifice. In this manner, the flow control system of FIGS. 28 and 29 allows the draw back of liquid in the flow line in a reverse direction during the exhalation phase of the ventilator when the liquid flow line is shut off.

Timing of Nebulization

[0080] As mentioned before, in order to deliver the nebulized medicine to the lungs, it is preferred that the medicine is carried by the inhalation of the patient. A number of factors affect the efficiency of the medicine delivered this way. The following embodiments are directed to improving drug delivery efficiency taking into account some of these factors.

[0081] If the patient is intubated, it may be possible to synchronize the timing of the nebulization pulse with the patient's ventilation. In one embodiment, this may be accomplished by providing an interface between the ventilator and the nebulizer. In some circumstances it may be preferred to provide other means for triggering the nebulization. For example, the ventilator being used may not provide a suitable interface. Also, the ventilator may not provide sufficiently accurate information concerning the patient's respiration to enable the nebulization catheter to operate with highest efficiency. In such situations, it may be preferred to utilize one or more separate sensors to obtain information that can be used to trigger and operate the nebulization catheter.

[0082] Referring to FIG. 30, there is a nebulizing catheter 944 positioned in an endotracheal tube 948 located in the trachea 952 of a patient. A proximal end of the endotracheal tube 948 is connected to a ventilator 956. In order to obtain physiological information concerning the patient's respiration for use in timing the generation of nebulization pulses by the nebulization catheter 944, one or more sensors may be used. For example, a first sensor 960 may be located on a distal end of the endotracheal tube 948. In addition, a sensor 964 may be positioned on the nebulization catheter 944. Another sensor 968 may be positioned on a separate device, such as a separate catheter 972 which is located further distally in the respiratory system. In addition, a sensor 976 may be positioned in the ventilator circuit of the ventilator 956 or in a ventilator auxiliary port, if available, or elsewhere on the patient. These sensors 960, 964, 968, and 976 may be types of sensors that measure pressure, flow or a physiological parameter of the patient, such as muscle contraction, electophysiological activity, etc. In alternative embodiments, one or more of these sensors may be used.

[0083] FIGS. 31 and 32 show alternative embodiments of nebulization catheters that incorporate sensors. In FIG. 31, a nebulization catheter 980 is shown. This nebulization catheter 980 may be similar to the nebulization catheter in FIG. 7. In FIG. 31, a main shaft 984 includes a plurality of lumens with a centrally located lumen 988 used to deliver a liquid medicine and a plurality of lumens 992 located peripherally around it used to deliver a pressurized gas. One of the peripheral lumens 996 is not used for pressurized gas delivery, but instead is used for sensing purposes. This may be accomplished by forming an aperture 1000 through a wall of the main shaft 984. The aperture communicates with the sensing lumen 996. The aperture 1000 may be open or may be covered with a flexible diaphragm that permits transmission of pressure across it. A pressure sensing device may be located at a proximal end of the nebulizing catheter. The pressure at the distal end of the nebulizing catheter can be sensed by the proximally located sensing device via the sensing lumen 996. This could rely on pneumatic sensing of the distal air pressure. Because of the effect of the distal gas pressurization orifice, pressure sensing through the sensing lumen 996 may be used for purposes of gross overpressure for safety purposes. Alternatively, the pressure sensing lumen 996 may be used during periods of time when a pressurizing gas is not being delivered to sense the patient's physiological airway pressure.

[0084] FIG. 32 shows another embodiment of a pressure sensing nebulization catheter. This embodiment is similar to the embodiment of FIG. 31 except that a sensor 1004 is located at a distal end of the catheter 980, specifically in the aperture 1000. In this embodiment, the sensor 1004 is a pressure transducer. Wire leads 1008 extend proximally from the sensor 1004 via the lumen 996. Instead of measuring pressure, the sensor 1004 could measure the flow at the distal end of the catheter. This may be accomplished by piezoelectric, optical, Hall effect, or other types of sensor technologies. The sensor may also be of a fiber optic type.

[0085] Although the embodiments of FIGS. 31 and 32 show sensing apparatuses associated with a nebulization catheter, these same types of sensors could also be used in the endotracheal tube 948, the separate catheter 972, or the ventilator 956 of FIG. 30 or the ventilator circuit.

[0086] The sensor outputs information to a controller 1012 that operates the flow control portion 1013 of the nebulization catheter system. The flow control portion may include the flow control assembly 872 (shown in FIG. 28) as well as include the control functions for gas pressurization. The controller 1012 may have preset triggering parameters or may be user adjustable. The controller 1012 may use airway flow, pressure, or physiological activity as a basis for controlling the flow control assembly 1013. The controller 1012 may provide for pulsing based upon any one of the following modes: (1) a controlled volume (bolus) of medicine is delivered with each pulse; (2) medicine is delivered until a physiological condition is sensed, e.g. exhalation; or (3) medicine is delivered for a fixable time interval, e.g. 2 seconds. These modes of operation may be selectable by the physician based upon the preferred treatment taking into account the patient's condition, the type of medicine being delivered, etc.

[0087] It may also be desired to regulate the delivery of aerosol so that it is not delivered with every inhalation. As mentioned above, one concern with delivery of an expanding gas is the cooling effect that it may have on the body. This can be a factor with high gas flow rates. Accordingly, it may be preferable to deliver aerosol on every other inhalation or every third inhalation, and so on. Alternatively, it may be preferred to deliver aerosol for certain periods of time, e.g. 5 minutes every hour. Therefore, by alternating aerosol delivery, the cooling effect associated with it can be reduced.

Alternative Embodiments

Nebulizing Catheter Incorporated in Endotracheal Tube

[0088] The various embodiments of nebulizing catheters, disclosed above, have been described as being either adapted for use in conjunction with a separate endotracheal tube, or adapted to be used without an endotracheal tube. If used with an endotracheal tube, the embodiments of the nebulizing catheter disclosed above are preferably removable from the endotracheal tube if one is present. It is noted that many of the embodiments of the present invention disclosed herein may also be used in conjunction with a nebulization catheter that is non-removable from an endotracheal tube, i.e. in which the nebulizing catheter is incorporated into and forms part of the endotracheal tube. An endotracheal tube that provides for nebulized medication delivery is described in a patent application filed by Dr. Neil R. MacIntyre on March 10, 1992 entitled "Endotracheal Tube Adapted for Aerosol Generation at Distal End Thereof", the entire disclosure of which is incorporated herein by reference. According to a system developed by Dr. MacIntyre, there is provided an endotracheal tube that provides for nebulization of a medication at a distal end thereof. According to Dr. MacIntryre's system, an endotracheal tube includes two additional, separate lumens, in addition to its main ventilation lumen used for the patient's breathing airflow. A medication in a liquid form is conveyed through one of the additional lumens and a pressurized gas is conveyed through the other lumen. The two additional lumens have distal openings near the distal end of the endotracheal tube airflow lumen. The distal opening of the pressurized gas lumen directs the pressurized gas across the distal medication lumen opening thereby nebulizing the liquid medication so that it can be delivered to the patient's lungs. It is intended that the present invention covers embodiments of nebulization catheters that are non-removable relative to an endotracheal tube.

Nebulizing Function Incorporated In Suction Catheter

[0089] As mentioned above, the nebulizing catheter can be incorporated into another device, such as an endotracheal tube, either removably or non-removably. Another such device into which a nebulizing catheter can be adapted is a suction or aspiration catheter. A suction catheter is sometimes used in conjunction with patients who are intubated. A suction catheter has an O. D. and a length such that it can be inserted through the ventilation lumen of an endotracheal tube. The suction catheter is used to aspirate fluids and mucin secretions that collect in the respiratory tract of in the endotracheal tube of a patient who is intubated. A conventional suction catheter is inserted down the ventilation lumen of the endotracheal tube and out the distal end. A mucolytic agent may be instilled as a liquid via a lumen of the suction catheter to help in the withdrawal of mucin from the trachea or bronchi. The suction catheter may then be withdrawn from the endotracheal tube and either disposed or retained in a sterile sheath connected to a proximal end of the endotracheal tube so that it can be reinserted into the endotracheal tube again.

[0090] A nebulizing catheter can be incorporated into a suction catheter so that a single device can perform both the functions of aspiration and nebulization for aerosol delivery. In an alternative embodiment of the present invention, the nebulizing catheter, such as described above, could be incorporated into a suction catheter so that a single catheter can provide both functions. This could be accomplished by provided any of the embodiments of the nebulization catheter described above with a separate lumen for the purpose of providing a suction to withdraw fluid from a patient's respiratory tract. Combining the functions of a suction catheter and nebulization catheter into a single device has the advantages of avoiding the expense of separate products as well as avoiding the inconvenience of inserting and withdrawing separate devices.

[0091] Suction catheters combined with a nebulization catheter are shown in FIGS. 33 - 40. FIGS. 33 - 37 show a suction catheter assembly 1220 including a suction catheter shaft 1222 slidably located inside of a flexible sheath 1224. A suction lumen 1226 extends through

the suction catheter shaft 1222. A proximal manifold 1226 includes a port 1228 for connecting a vacuum source to the suction catheter lumen 1225. A valve 1230 operates to open and close the port 1228. A distal sleeve 1232 provides for connecting to an endotracheal tube such that the suction catheter shaft 1222 can be inserted into the endotracheal tube by pushing the proximal manifold 1226 toward the distal sleeve 1232. The distal sleeve 1232 may include a manifold for connection to a flush port 1233. A seal 1235 located in the sleeve 1232 closely bears on the suction catheter shaft to remove mucous or other unwanted materials that can be removed via the flush port 1233. The shaft of the suction catheter may be provided with a low friction, e.g. hydrophilic, coating to reduce adhesion of mucous.

[0092] The suction catheter assembly 1220 includes two additional lumens 1234 and 1236. These lumens 1234 and 1236 are located in a wall of the suction catheter shaft 1222. These lumens 1234 and 1236 communicate with distal orifices 1238 and 1240 located at a distal end of the suction catheter shaft 1222. These lumens 1234 and 1236 are used to deliver a liquid medicine and a pressurized gas for nebulizing the liquid medicine, as described above. Also located at a distal end of the suction catheter shaft 1222 are suction openings 1242.

[0093] The suction catheter assembly 1220 can be used in a conventional manner to remove mucin from the trachea and from the bronchi. The suction catheter assembly 1220 can also be used to deliver medicines to the lungs as an aerosol by means of the nebulizing lumens 1234 and 1236. The nebulizing lumens can also be used to deliver mucolytic agents as an aerosol. Because the fine aerosol delivered by the nebulizing lumens can be carried by a patient's inspiratory airflow into the bronchi, the mucolytic agent can be delivered further into bronchi compared to a suction catheter that merely instills or generates a coarse spray of a mucolytic agent. In addition, the flow velocity produced by the gas pressurization lumen may be used to assist in breaking up mucous at the end of the suction catheter.

[0094] When using the suction catheter assembly 1220, it can be positioned so that a distal end of the suction catheter shaft 1222 is close to the distal end of the endotracheal tube 1250 as shown in FIG. 35 or alternatively the suction catheter shaft 1222 can be positioned so that it extends past the distal end of the endotracheal tube 1250 as shown in FIG. 37. As shown in FIG. 37, the suction catheter shaft 1220 may be formed with a distal curvature so that the distal end can be brought into proximity with the tracheal wall.

[0095] Rather than incorporate the nebulizing lumens into the wall of the suction catheter, it may be preferably in many situations to use a conventional suction catheter with a stand-alone nebulizing catheter. The stand-alone nebulizing catheter may be similar to any of the embodiments described above. A suction catheter and a nebulizing catheter can readily be used together with the alternative versions of the manifolds shown in FIGS. 38 - 40

[0096] Referring to FIG. 38, an endotracheal tube 1252 has a proximal end with a single port 1254. A suction catheter 1256 has a distal manifold 1258. The distal manifold 1256 could be formed as part of the suction catheter 1256 or could be provided as a separate component. The suction catheter manifold 1258 connects to the single port 1254 of the endotracheal tube 1252. The manifold 1258 has a first port 1260 for connecting to a ventilator and a second port 1264 for connecting to a proximal end of a nebulizing catheter 1266. As shown in FIG. 38, the nebulizing catheter 1266 includes a sterile sheath 1268 which is similar to the sheath included on the suction catheter 1262. In the embodiment of FIG. 38, the suction catheter 1256 and the nebulizing catheter 1266 are positioned alternately inside the ventilation lumen of the endotracheal tube 1252. The suction catheter or the nebulizing catheter can be withdrawn temporarily and maintained in its sterile sheath while the other is being used.

[0097] Referring to FIG. 39 there is shown another arrangement for connecting a suction catheter and nebulizing catheter to an endotracheal tube. In this embodiment, a manifold 1270 connects to the proximal end of the endotracheal tube 1252. The manifold 1270 has port 1274 for receiving the nebulizing catheter 1266 and a second port 1276. A distal manifold 1278 of a suction catheter 1280 connects to the second port 1276. The suction catheter manifold 1278 has a port 1282 for connecting to the ventilator. This arrangement can be used similarly to the arrangement of FIG. 38.

[0098] FIG. 40 shows still another arrangement for connecting a suction catheter and a nebulizing catheter to an endotracheal tube. In this embodiment, the endotracheal tube 1252 is provided with a proximal end that includes dual ports. A first port 1284 receives the nebulizing catheter 1266. The second port 1286 may be connected to either directly to a ventilator or may be connected to a distal end of a suction catheter (not shown) in a conventional manner.

[0099] In another alternative embodiment (not shown), the nebulizing catheter could be positioned down the suction lumen of the suction catheter.

[0100] FIG. 41 shows another suction catheter also incorporating a nebulization of an aerosol. In FIG. 41, a suction catheter 1400 is extends from the ventilation lumen of an endotracheal tube 1250. The suction catheter 1400 includes distal suction orifices 1402 located close to the distal end of the suction catheter shaft. Located along the suction catheter shaft proximally of the suction orifices 1402 are one or more pairs of liquid and gas orifices 1404. The liquid and gas orifice pairs 1404 are located with respect to each other to produce an aerosol of the liquid being delivered to the liquid orifice as in the previous embodiments. The nebulization orifices 1404 are oriented radially from the suction catheter shaft to direct the aerosol delivered from the nebulization orific-

es 1404 toward the airway passage wall. The aerosol being delivered may be a mucolytic agent. The suction provided by the suction orifices draws the mucolytic agent delivered from the nebulization orifices as well as mucous treated by the mucolytic agent in a distal direction into the suction orifices 1402.

[0101] Another suction catheter with aerosol delivery is shown in FIG. 42. A suction catheter 1410 is located in a ventilation lumen of the endotracheal tube 1250. As in the previous embodiment, the suction catheter 1410 has a distal suction orifice 1412 for removing mucous from the airway passage. In addition, the suction catheter 1410 also includes distal gas and liquid orifices 1414 located in proximity to each other to produce a aerosol. The liquid and gas orifices are located in a distal extension 1416 of the suction catheter shaft so that they are distal of the suction orifice 1412. The liquid and gas nebulization orifices 1414 are oriented in a proximal direction toward the suction orifice 1412. The distal extension 1416 is formed to bring the nebulization orifices 1414 close to the wall of airway passage so that the aerosol delivered from the nebulization orifices 1414 washes the airway passage wall. As in the previous catheter, the aerosol delivered may be a mucolytic agent to facilitate suctioning of the mucous out of the airway passage. The pressurized gas flow may be used to contribute to the dislodgement of mucous from the airway passage walls.

Other Method for Aerosol Generation

[0102] The above embodiments describe a nebulization catheter in which an aerosol is generated by directing a pressurized gas through a catheter near an orifice from which the liquid to be nebulized exits. It is considered to be within the scope of the invention described herein to use other means or agents to generate an aerosol for delivery of a medication to the respiratory tract. For example, the above embodiments may be used in conjunction with devices that utilize other means to generate an aerosol of a liquid medication. A liquid delivered by a single liquid lumen may be nebulized by applying ultrasonic energy to the liquid, electrospray, steam, or a micropump similar to those used in ink jet type printers. These approaches to nebulization may be combined with pressurized gas to produce an aerosol of the liquid medication.

[0103] . The nebulization catheter embodiments described herein could also be used in other types of nebulizers that are used externally of a patient's respiratory system, such as small volume nebulizers (SVN), humidification nebulizers, or nebulizers used for ocular or nasal drug administration. When used in such other types of nebulizers, the embodiments of the nebulization catheter disclosed herein provide for a fine aerosol without the potential disadvantages of impacting the liquid on a baffle or recirculating the liquid medicine on a continuous basis which are common in such nebulizers.

[0104] It is intended that the foregoing detailed description be regarded as illustrative rather than limiting and that it is understood that the following claims define the scope of the invention.

Claims

1. A catheter for delivering an aerosol of medicine to a patient's lungs, the catheter comprising:

    a catheter shaft (132) having:

    a liquid lumen (134) centrally located in said shaft and adapted for conveying a medicine in liquid form;
    a plurality of gas lumens (135) peripherally located around said liquid lumen (134) and adapted for conveying a gas;
    a distal liquid orifice (139) communicating with said liquid lumen (134); and
    a plurality of distal gas orifices communicating with said plurality of gas lumens (135), said plurality of gas orifices being aligned with respect to said distal liquid orifice (139) so as to nebulize a liquid medicine discharged from the liquid orifice (139).

2. A catheter as claimed in Claim 1 **characterised in that** at least a portion (141) of said shaft (136) surrounding said liquid lumen (137) is formed of a low compliance material so that flow control at said distal liquid orifice (139) of a fluid delivered through said liquid lumen (137) is more responsive to flow control at a location proximal thereto.

3. A catheter as claimed in Claim 1 or 2, further **characterised by** including a tip region (160) formed by a taper in the distal end of the catheter.

4. A catheter as claimed in Claim 3, **characterised in that** the distal end (156) of the catheter (148) is in the form of a tip region (160) that is tapered such that the lumens (164, 168) are in closer proximity to each other at a distal end of said tip region (160) than at a proximal end of the tip region and/or the respective internal diameter of the lumens (164, 168) is smaller at a distal end of the tip region (160) than at a proximal end of the tip region (160).

5. A catheter as claimed in Claim 3 or 4, **characterised in that** six said gas orifices (168) surround said liquid orifice (164); and six said gas lumens are congruent with the six gas orifices (168).

6. A catheter as claimed in Claim 3, 4 or 5, **characterised in that** the liquid orifice (164) has a diameter

of approximately 0.051mm (0.002 inches).

7. A catheter as claimed in any one of Claims 3 to 6, **characterised in that** each gas orifice (168) has a diameter of 0.051mm (0.002 inches).

8. A catheter as claimed in Claim 1, **characterised by** a proximal shaft section (176) and a distal shaft section (180); and a plurality of lumens (184) in said proximal shaft section (176).

9. A catheter as claimed in Claim 8 further **characterised by**:

   a distal end of the proximal shaft section (176) connected to the proximal end of the distal shaft section (180);
   a tapered cavity (192) formed between said distal end of said distal shaft section (180) and said distal end of said proximal shaft section;
   a distal orifice (196) located at the distal end of the distal shaft section (180); and
   a tubular extension (200) extending the central lumen used to convey a liquid through the tapered cavity (192) and out said distal orifice (196); and
   wherein said distal orifice (196) is sized to permit gas flow in an annular region around the tubular extension (200) to nebulize the liquid that exits the distal orifice of the tubular extension.

10. A catheter as claimed in Claim 9, **characterised in that** the distal orifice has an interior diameter of 0.635mm (0.25 inches).

11. A catheter as claimed in Claim 9 or 10 **characterised in that** the tubular extension has an outer diameter of 0.305mm (0.012 inches) and an inner diameter of 0.178mm (0.007 inches).

12. A catheter as claimed in any one of Claims 8 to 11 **characterised in that** the distal shaft section (180) is composed of stainless steel.

13. A catheter as claimed in any one of the preceding claims, **characterised by** a tapered wire (212) located with respect to the liquid orifice (216) so that liquid from the liquid lumen continues to flow distally of the distal liquid orifice (216) along the wire (212).

14. A catheter as claimed in Claim 13, **characterised in that** the wire (240) has a curved shape such that gas from the gas orifices causes the wire to whip round in a spiral motion.

15. A catheter as claimed in Claim 1 further **characterised by** a porous plug (142) located in said liquid orifice (139).

16. A catheter as claimed in any one of Claims 1 to 12 **characterised by** a tapered wire or filament (240) for increasing the width of the aerosol.

17. A catheter as claimed in Claim 1, **characterised by** a peripherally located lumen (996) which is used for sensing purposes.

18. An apparatus for delivering an aerosol of medicine to a patient's lungs **characterised by** comprising a catheter as claimed in any one of the preceding claims:

   the catheter shaft having a proximal end and a distal end;
   the liquid lumen communicating at the proximal end with a port (32) for receiving a medicine in a liquid form;
   a flow control apparatus connected to the port (32), said flow control apparatus comprising:

      a flow line (876) communicating with the port (32), said flow line occupied by the medicine; and
      a valve (868) associated with the flow line to cause pulsed delivery of medicine through the flow line.

19. A catheter or apparatus as claimed in any one of the preceding claims **characterised by** further comprising a safety stop (44) on a proximal portion of the catheter shaft.

20. A catheter or apparatus as claimed in any one of the preceding claims **characterised by** further comprising graduated markings (41) on said catheter shaft.

21. A catheter or apparatus as claimed in any one of the preceding claims **characterised by** further comprising luer lock connectors on proximal ports communicating with said gas lumens and said liquid lumen.

22. A catheter or apparatus as claimed in any one of the preceding claims **characterised by** further comprising a stripe (43) on said catheter shaft.

23. A catheter or apparatus as claimed in any one of the preceding claims **characterised in that** said catheter shaft (340) includes a further lumen (368) extending therethrough; and
   a fiber optic scope (366) extending through said further lumen.

24. A suction catheter for use with an endotracheal tube, said suction catheter sized to be received in a ventilation lumen of the endotracheal tube, said

suction catheter having an aspiration lumen for removing mucous from the respiratory tract of an intubated patient; said suction catheter being **characterised by** further incorporating a nebulization catheter as claimed in any one of the preceding claims.

25. A method of forming the catheter of any one of Claims 3 to 7, the catheter having closely spaced distal orifices sized and spaced apart with low tolerances, comprising the steps of:

providing a relatively large size multilumen extruded polymer tubing;
heating a portion of the tubing to a transition temperature of said tubing;
drawing down said portion of tubing to form a tapered section with a draw down ratio in the range between 2 to 1 and 20 to 1 such that the lumens are increasingly closely spaced in said tapered region; and
forming a plurality of orifices at a distal end of said tapered section, said plurality of orifices being sized to nebulize a liquid delivered through one of said lumens to form an aerosol with a gas delivered through others of said lumens.

26. A method as claimed in Claim 25 **characterised in that** the step of forming a plurality of orifices further comprises:

cutting a distal end of the tapered section.

27. A method as claimed in Claim 25 further **characterised by** cutting the tubing to size to form a shaft portion of the nebulization catheter.

28. A method as claimed in Claim 25 further **characterised by** exposing a portion of said tubing to high energy radiation.

29. A method as claimed in Claim 25 **characterised in that** the step of heating further comprises heating the tubing to a temperature between a melt state and a glass state of said tubing.

Patentansprüche

1. Katheter zur Abgabe eines Arzneimittelaerosols an die Lungen eines Patienten, wobei der Katheter Folgendes umfasst:

einen Katheterschaft (132), aufweisend:

ein Flüssigkeitslumen (134), das im Schaft mittig angeordnet ist und zur Förderung eines Arzneimittels in flüssiger Form ausgelegt ist;
eine Vielzahl von Gaslumen (135), die auf dem Umfang um das Flüssigkeitslumen (134) herum angeordnet ist und zur Förderung eines Gases ausgelegt ist;
eine distale Flüssigkeitsöffnung, die mit dem Flüssigkeitslumen (134) kommuniziert; und
eine Vielzahl von distalen Gasöffnungen, die mit der Vielzahl von Gaslumen (135) kommuniziert, wobei die Vielzahl von Gasöffnungen zur distalen Flüssigkeitsöffnung ausgerichtet ist, damit ein flüssiges, aus der Flüssigkeitsöffnung gefördertes Arzneimittel zerstäubt wird.

2. Katheter nach Anspruch 1, **dadurch gekennzeichnet, dass** mindestens ein Teil (141) des Schaftes (136), der das Flüssigkeitslumen (137) umgibt, aus einem Material mit geringer Nachgiebigkeit geformt ist, so dass die Durchflusssteuerung an der distalen Flüssigkeitsöffnung (139) für eine durch das Flüssigkeitslumen (137) geförderte Flüssigkeit gegenüber der Durchflusssteuerung an einem dazu proximalen Ort empfindlicher ist.

3. Katheter nach Anspruch 1 oder 2, außerdem **dadurch gekennzeichnet, dass** er einen Spitzenbereich (160), der durch einen Konus im distalen Ende des Katheters gebildet wird, umfasst.

4. Katheter nach Anspruch 3, **dadurch gekennzeichnet, dass** das distale Ende (156) des Katheters (148) die Form eines Spitzenbereiches (160) aufweist, der konisch derart ausgeführt ist, dass die Lumen (164, 168) an einem distalen Ende des Spitzenbereiches (160) näher beieinander liegen als an einem proximalen Ende des Spitzenbereiches und/oder der jeweilige Innendurchmesser der Lumen (164, 168) an einem distalen Ende des Spitzenbereiches (160) kleiner ist als an einem proximalen Ende des Spitzenbereiches (160).

5. Katheter nach Anspruch 3 oder 4, **dadurch gekennzeichnet, dass** die Flüssigkeitsöffnung (164) von sechs der Gasöffnungen (168) umgeben ist; und sechs der Gaslumen mit den sechs Gasöffnungen (168) deckungsgleich sind.

6. Katheter nach Anspruch 3, 4 oder 5, **dadurch gekennzeichnet, dass** die Flüssigkeitsöffnung (164) einen Durchmesser von ungefähr 0,051 mm (0,002 inches) aufweist.

7. Katheter nach einem der Ansprüche 3 bis 6, **dadurch gekennzeichnet, dass** jede Gasöffnung (168) einen Durchmesser von 0,051 mm (0,002

inches) aufweist.

8. Katheter nach Anspruch 1, **gekennzeichnet durch** einen proximalen Schaftabschnitt (176) und einen distalen Schaftabschnitt (180); und eine Vielzahl von Lumen (184) im proximalen Schaftabschnitt (176).

9. Katheter nach Anspruch 8, der außerdem **gekennzeichnet ist durch**:

   ein distales Ende des proximalen Schaftabschnittes (176), der mit dem proximalen Ende des distalen Schaftabschnittes (180) verbunden ist;
   einen konischen Hohlraum (192), der zwischen dem distalen Ende des distalen Schaftabschnittes (180) und dem distalen Ende des proximalen Schaftabschnittes ausgebildet ist;
   eine distale Öffnung (196), die sich am distalen Ende des distalen Schaftabschnittes (180) befindet; und
   ein röhrenförmiges Ansatzstück (200), welches das mittige Lumen verlängert und eingesetzt wird, um eine Flüssigkeit durch den konischen Hohlraum (192) und aus der distalen Öffnung (196) zu fördern; und
   wobei die distale Öffnung (196) so bemessen ist, dass ein Gasdurchfluss in einem ringförmigen Bereich um das röhrenförmige Ansatzstück (200) zum Zerstäuben der Flüssigkeit, die aus der distalen Öffnung des röhrenförmigen Ansatzstückes austritt, möglich ist.

10. Katheter nach Anspruch 9, **dadurch gekennzeichnet**, dass die distale Öffnung einen Innendurchmesser von 0,635 mm (0,25 inches) aufweist.

11. Katheter nach Anspruch 9 oder 10, **dadurch gekennzeichnet**, dass das röhrenförmige Ansatzstück einen Außendurchmesser von 0,305 mm (0,012 inches) und einen Innendurchmesser von 0,178 mm (0,007 inches) aufweist.

12. Katheter nach einem der Ansprüche 8 bis 11, **dadurch gekennzeichnet**, dass der distale Schaftabschnitt (180) aus nicht rostendem Stahl besteht.

13. Katheter nach einem der vorhergehenden Ansprüche, **gekennzeichnet durch** einen konisch ausgeführten Draht (212), der zur Flüssigkeitsöffnung (216) so angeordnet ist, dass die Flüssigkeit aus dem Flüssigkeitslumen in distaler Richtung aus der distalen Flüssigkeitsöffnung (216) längs des Drahtes (212) weiterfließt.

14. Katheter nach Anspruch 13, **dadurch gekennzeichnet**, dass der Draht (240) eine derart gekrümmte Form aufweist, dass Gas aus den Gasöffnungen das Herumschlagen des Drahtes in einer Spiralbewegung bewirkt.

15. Katheter nach Anspruch 1, außerdem **gekennzeichnet durch** einen porösen Stopfen (142), der sich in der Flüssigkeitsöffnung (139) befindet.

16. Katheter nach einem der Ansprüche 1 bis 12, **gekennzeichnet durch** einen konisch ausgeführten Draht oder Faden (240), der zur Vergrößerung der Breite des Aerosols dient.

17. Katheter nach Anspruch 1, **gekennzeichnet durch** ein auf dem Umfang angeordnetes Lumen (996), das zu Erfassungszwecken dient.

18. Apparat zur Abgabe eines Arzneimittelaerosols an die Lungen eines Patienten, **dadurch gekennzeichnet**, dass er einen Katheter nach einem der vorhergehenden Ansprüche umfasst:

   den Katheterschaft, der ein proximales Ende und ein distales Ende aufweist;

   das Flüssigkeitslumen, das am proximalen Ende mit einem Anschluss (32) zur Aufnahme eines Arzneimittels in einer flüssigen Form kommuniziert;

   ein Durchflusssteuerungsapparat, der mit dem Anschluss (32) verbunden ist, wobei der Durchflusssteuerungsapparat Folgendes umfasst:

      eine Durchflussleitung (876), die mit dem Anschluss (32) kommuniziert, wobei die Durchflussleitung von dem Arzneimittel eingenommen wird; und

      ein Ventil (888), das mit der Durchflussleitung assoziiert ist, um eine gepulste Abgabe des Arzneimittels über die Durchflussleitung zu bewirken.

19. Katheter oder Apparat nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet**, dass dieser außerdem einen Sicherheitsanschlag (44) an einem proximalen Teil des Katheterschaftes umfasst.

20. Katheter oder Apparat nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet**, dass dieser außerdem Messmarkierungen (41) am Katheterschaft umfasst.

21. Katheter oder Apparat nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet**, dass dieser Luer-Lock-Ansätze an proximalen An-

schlüssen umfasst, die mit den Gaslumen und dem Flüssigkeitslumen kommunizieren.

22. Katheter oder Apparat nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet,** dass er außerdem einen Streifen (43) am Katheterschaft umfasst.

23. Katheter oder Apparat nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet,** dass der Katheterschaft (340) ein weiteres Lumen (368) umfasst, das durch ihn verläuft; sowie
ein Glasfaserskop (366), das sich durch das weitere Lumen erstreckt.

24. Absaugkatheter für den Einsatz mit einem Endotrachealtubus, wobei der Absaugkatheter so bemessen ist, dass er in ein Beatmungslumen des Endotrachealtubus passt und der Absaugkatheter ein Absauglumen zur Entfernung von Schleim aus dem Atemtrakt eines intubierten Patienten aufweist; wobei der Absaugkatheter durch den zusätzlichen Einbau eines Katheters mit Zerstäubungseinrichtung nach einem der vorhergehenden Ansprüche gekennzeichnet ist.

25. Verfahren zur Formgebung des Katheters nach einem der Ansprüche 3 bis 7, wobei der Katheter distale Öffnungen mit kleinen Abständen aufweist, für deren Abmessungen und Abstände geringe Toleranzen zur Anwendung kommen, umfassend die folgenden Schritte:

Bereitstellen einer relativ großen, extrudierten Polymer-Multilumen-Schlauchleitung;
Aufheizen eines Teils der Schlauchleitung auf eine Übergangstemperatur der Schlauchleitung;
Auslängen dieses Teils der Schlauchleitung, um einen konischen Abschnitt mit einem Reckverhältnis im Bereich zwischen 2 bis 1 und 20 bis 1 zu formen, so dass die Lumen einen zunehmend kleineren Abstand im konischen Bereich aufweisen; und
Formen einer Vielzahl von Öffnungen an einem distalen Ende des konischen Abschnittes, wobei die Vielzahl von Öffnungen für die Zerstäubung einer Flüssigkeit, die durch eines der Lumen gefördert wird, ausgelegt ist, damit ein Aerosol mit einem Gas gebildet wird, das durch die anderen Lumen gefördert wird.

26. Verfahren nach Anspruch 25, **dadurch gekennzeichnet,** dass der Schritt zum Formen einer Vielzahl von Öffnungen außerdem Folgendes umfasst:

das Schneiden eines distalen Endes des konischen Abschnittes.

27. Verfahren nach Anspruch 25, das außerdem **gekennzeichnet ist durch** den Zuschnitt der Schlauchleitung, um einen Schaftteil des Katheters mit Zerstäubungseinrichtung zu formen.

28. Verfahren nach Anspruch 25, außerdem **gekennzeichnet durch** die Bestrahlung eines Teils der Schlauchleitung mit energiereicher Strahlung.

29. Verfahren nach Anspruch 25 **dadurch gekennzeichnet,** dass der Schritt des Aufheizens außerdem das Aufheizen der Schlauchleitung auf eine Temperatur zwischen einem Schmelzzustand und einem Glaszustand der Schlauchleitung umfasst.

Revendications

1. Cathéter pour délivrer un médicament en aérosol aux poumons d'un patient, le cathéter comprenant:

une tige de cathéter (132) comportant:

une lumière de passage de liquide (134) située au centre de ladite tige et conçue pour transporter un médicament sous forme liquide;

une pluralité de lumières de passage de gaz (135) situées sur la périphérie entourant ladite lumière de passage de liquide (134) et conçues pour transporter un gaz;

un orifice distal de passage de liquide communiquant avec ladite lumière de passage de liquide (134); et

une pluralité d'orifices distaux de passage de gaz communiquant avec ladite pluralité de lumières de passage de gaz (135), ladite pluralité d'orifices de passage de gaz étant alignée par rapport audit orifice distal de passage de liquide de façon à nébuliser un médicament liquide déchargé de l'orifice de passage de liquide.

2. Cathéter selon la revendication 1, **caractérisé en ce qu'**au moins une partie (141) de ladite tige (136) entourant ladite lumière de passage de liquide (137) est formée à partir d'un matériau de faible complaisance de sorte que la régulation de débit au niveau dudit orifice distal de passage de liquide (139) d'un fluide délivré à travers ladite lumière de passage de liquide (137) est plus sensible à la régulation de débit à un emplacement qui lui est proximal.

3. Cathéter selon la revendication 1 ou 2, **caractérisé**

en outre en ce qu'il comprend une zone de pointe (160) formée par un cône dans l'extrémité distale du cathéter.

4. Cathéter selon la revendication 3, caractérisé en ce que l'extrémité distale (156) du cathéter (148) présente la forme d'une zone de pointe (160) qui est conique de sorte que les lumières (164, 168) sont à proximité plus étroite les unes des autres à une extrémité distale de ladite zone de pointe (160) qu'à une extrémité proximale de la zone de pointe et/ou le diamètre interne respectif des lumières (164, 168) est plus petit à une extrémité distale de la zone de pointe (160) qu'à une extrémité proximale de la zone de pointe (160).

5. Cathéter selon la revendication 3 ou 4, caractérisé en ce que six dits orifices de passage de gaz (168) entourent ledit orifice de passage de liquide (164); et six dites lumières de passage de gaz sont congruentes avec les six orifices de passage de gaz (168).

6. Cathéter selon la revendication 3, 4 ou 5, caractérisé en ce que l'orifice de passage de liquide (164) a un diamètre d'approximativement 0,051 mm (0,002 pouce).

7. Cathéter selon l'une quelconque des revendications 3 à 6, caractérisé en ce que chaque orifice de passage de gaz (168) a un diamètre de 0,051 mm (0,002 pouce).

8. Cathéter selon la revendication 1, caractérisé par une section de tige proximale (176) et une section de tige distale (180); et une pluralité de lumières (184) dans ladite section de tige proximale (176).

9. Cathéter selon la revendication 8, caractérisé en outre par:

   une extrémité distale de la section de tige proximale (176) raccordée à l'extrémité proximale de la section de tige distale (180);

   une cavité effilée (192) formée entre ladite extrémité distale de ladite section de tige distale (180) et ladite extrémité distale de ladite section de tige proximale;

   un orifice distal (196) situé à l'extrémité distale de la section de tige distale (180); et

   un prolongement tubulaire (200) prolongeant la lumière centrale, utilisé pour transporter un liquide à travers la cavité effilée (192) hors dudit orifice distal (196); et

   dans lequel ledit orifice distal (196) est dimensionné pour permettre l'écoulement de gaz dans une zone annulaire entourant le prolongement tubulaire (200) de façon à nébuliser le liquide qui sort de l'orifice distal du prolongement tubulaire.

10. Cathéter selon la revendication 9, caractérisé en ce que l'orifice distal a un diamètre intérieur de 0,635 mm (0,25 pouce).

11. Cathéter selon la revendication 9 ou 10, caractérisé en ce que le prolongement tubulaire a un diamètre extérieur de 0,305 mm (0,012 pouce) et un diamètre intérieur de 0,178 mm (0,007 pouce).

12. Cathéter selon l'une quelconque des revendications 8 à 11, caractérisé en ce que la section de tige distale (180) est réalisée en acier inoxydable.

13. Cathéter selon l'une quelconque des revendications précédentes, caractérisé par un fil effilé (212) situé par rapport à l'orifice de passage de liquide (216) de sorte que le liquide provenant de la lumière de passage de liquide continue de s'écouler distalement par rapport à l'orifice distal de passage de liquide (216) le long du fil (212).

14. Cathéter selon la revendication 13, caractérisé en ce que le fil (240) présente une forme courbe de sorte que le gaz provenant des orifices de passage de gaz amène le fil à s'enrouler en fouettant en un mouvement spiralé.

15. Cathéter selon la revendication 1, caractérisé en outre par un bouchon poreux (142) situé dans ledit orifice de passage de liquide (139).

16. Cathéter selon l'une quelconque des revendications 1 à 12, caractérisé par un fil effilé ou filament (240) destiné à accroître la largeur de l'aérosol.

17. Cathéter selon la revendication 1, caractérisé par une lumière située en périphérie (996) qui est utilisée dans un but de détection.

18. Appareil pour délivrer un médicament en aérosol aux poumons d'un patient, caractérisé en ce qu'il comprend un cathéter selon l'une quelconque des revendications précédentes:

   la tige de cathéter comportant une extrémité proximale et une extrémité distale;

   la lumière de passage de liquide communiquant à l'extrémité proximale avec un orifice (32) pour recevoir un médicament sous forme liquide;

un appareil de régulation de débit raccordé à l'orifice (32), ledit appareil de régulation de débit comprenant:

un conduit d'écoulement (876) communiquant avec l'orifice (32), ledit conduit d'écoulement étant occupé par le médicament; et
une soupape (886) associée au conduit d'écoulement pour provoquer une délivrance pulsée de médicament à travers le conduit d'écoulement.

19. Cathéter ou appareil selon l'une quelconque des revendications précédentes, **caractérisé en ce qu'il** comprend en outre une butée de sécurité (44) sur une partie proximale de la tige de cathéter.

20. Cathéter ou appareil selon l'une quelconque des revendications précédentes, **caractérisé en ce qu'il** comprend en outre des repères gradués (41) sur ladite tige de cathéter.

21. Cathéter ou appareil selon l'une quelconque des revendications précédentes, **caractérisé en ce qu'il** comprend en outre des raccords de type Luer sur les orifices proximaux communiquant avec lesdites lumières de passage de gaz et ladite lumière de passage de liquide.

22. Cathéter ou appareil selon l'une quelconque des revendications précédentes, **caractérisé en ce qu'il** comprend en outre un filet (43) sur ladite tige de cathéter.

23. Cathéter ou appareil selon l'une quelconque des revendications précédentes, **caractérisé en ce que** ladite tige de cathéter (340) comprend une lumière supplémentaire (368) s'étendant à travers elle; et
un scope à fibre optique (366) s'étendant à travers ladite lumière supplémentaire.

24. Cathéter d'aspiration devant être utilisé avec un tube endotrachéal, ledit cathéter d'aspiration étant dimensionné pour être reçu dans une lumière de ventilation du tube endotrachéal, ledit cathéter d'aspiration comportant une lumière d'aspiration pour retirer les glaires des voies respiratoires d'un patient intubé; ledit cathéter d'aspiration étant **caractérisé en ce qu'il** comprend en outre un cathéter de nébulisation selon l'une quelconque des revendications précédentes.

25. Procédé de formation du cathéter selon l'une quelconque des revendications 3 à 7, le cathéter comportant des orifices distaux étroitement espacés, dimensionnés et espacés avec de petites tolérances, comprenant les étapes consistant à:

prévoir un tube polymère extrudé à plusieurs lumières de taille relativement grande;

chauffer une partie du tube à une température de transition dudit tube;

étirer ladite partie de tube pour former une section conique avec un rapport d'étirage dans la plage comprise entre 2 sur 1 et 20 sur 1, de sorte que les lumières sont de plus en plus étroitement espacées dans ladite zone conique; et

former une pluralité d'orifices à une extrémité distale de ladite section conique, ladite pluralité d'orifices étant dimensionnée pour nébuliser un liquide délivré à travers l'une desdites lumières afin de former un aérosol avec un gaz délivré à travers les autres desdites lumières.

26. Procédé selon la revendication 25, **caractérisé en ce que** l'étape consistant à former une pluralité d'orifices comprend en outre l'étape consistant à:

couper une extrémité distale de la section conique.

27. Procédé selon la revendication 25, **caractérisé en outre par** l'étape consistant à couper le tube à dimension pour former une partie de tige du cathéter de nébulisation.

28. Procédé selon la revendication 25, **caractérisé en outre par** l'étape consistant à exposer une partie dudit tube à un rayonnement d'énergie élevée.

29. Procédé selon la revendication 25, **caractérisé en ce que** l'étape de chauffage comprend en outre l'étape consistant à chauffer le tube à une température entre un état de fusion et un état vitreux dudit tube.

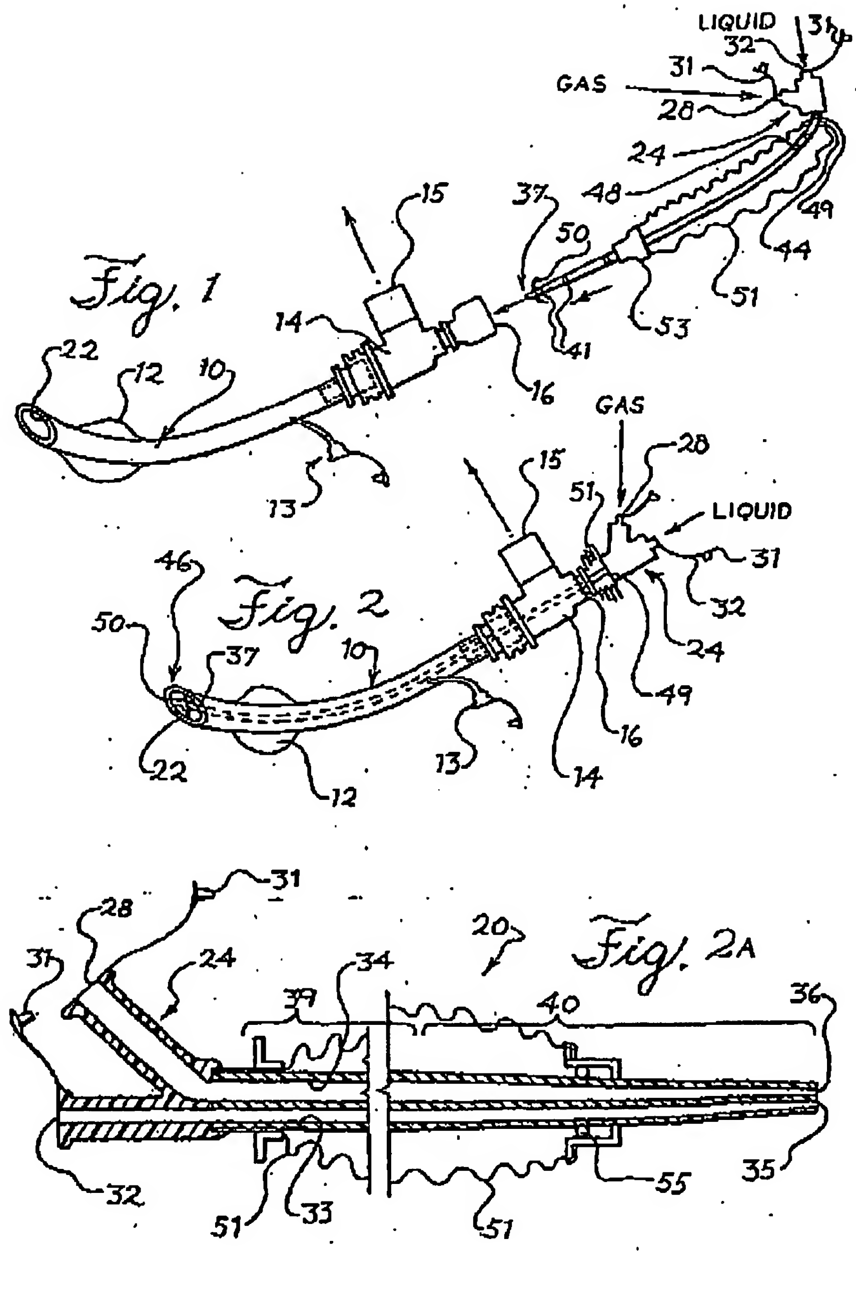


Fig. 1
LIQUID
GAS
Fig. 2
GAS
LIQUID
Fig. 2A

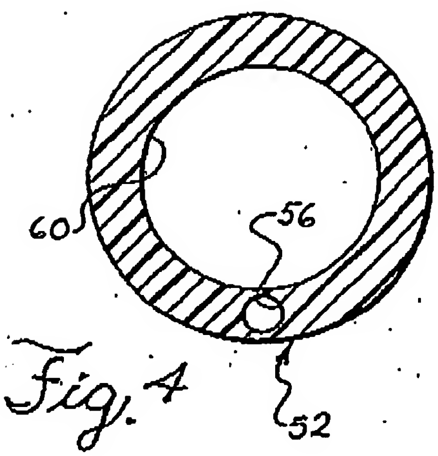


Fig. 4

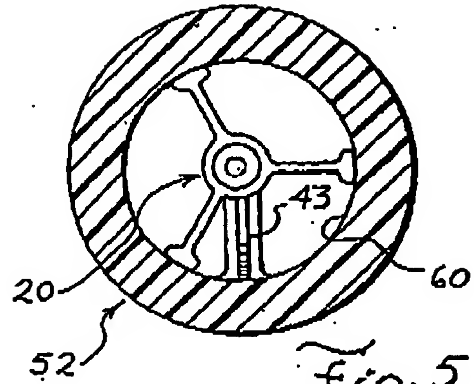


Fig 5

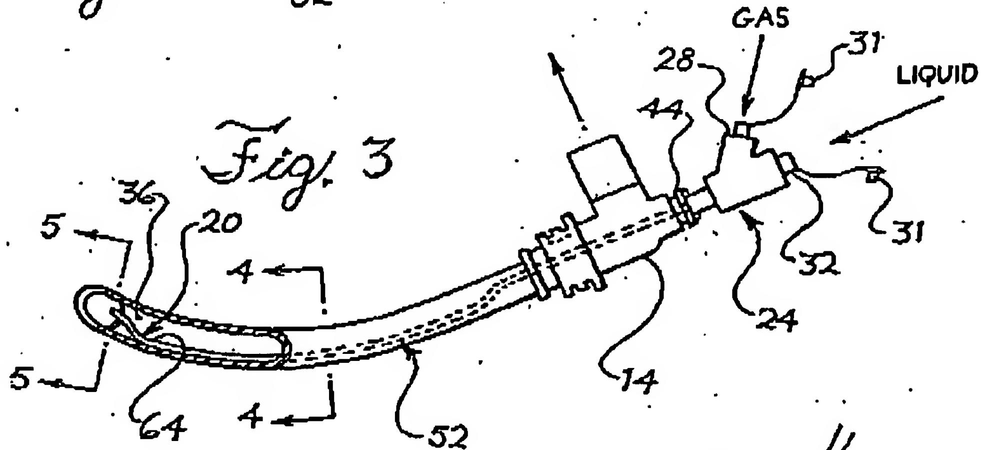


Fig. 3

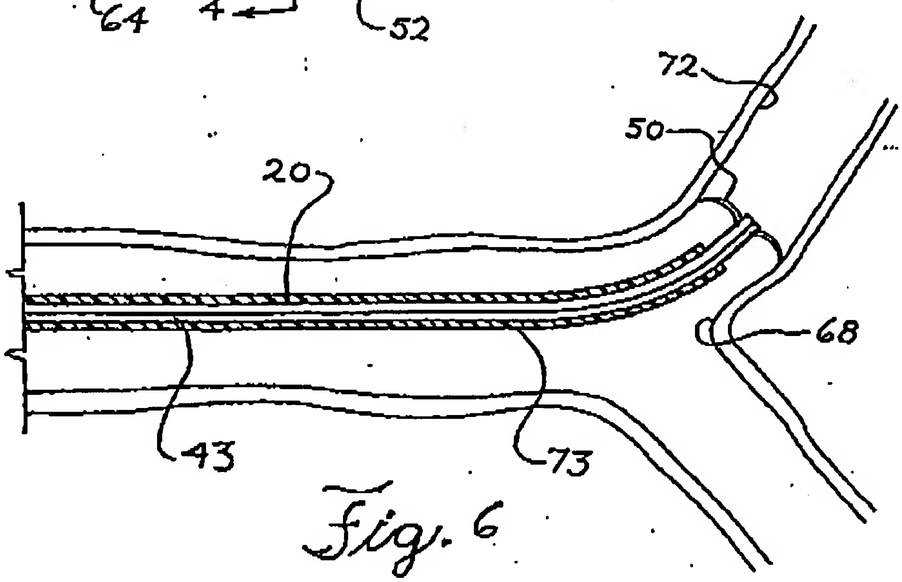


Fig. 6

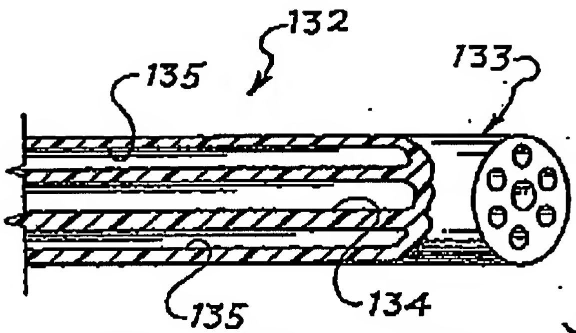


Fig. 7

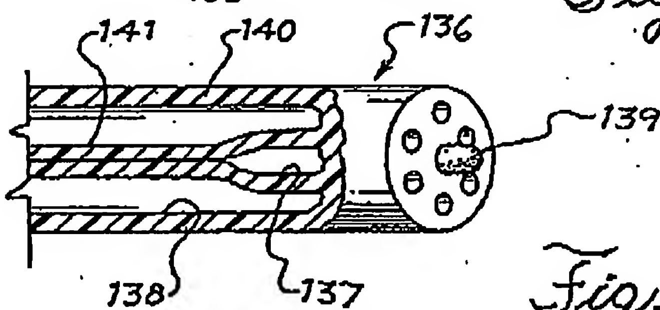


Fig. 8

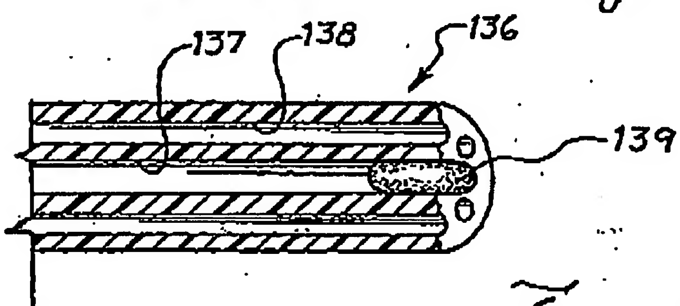


Fig. 9

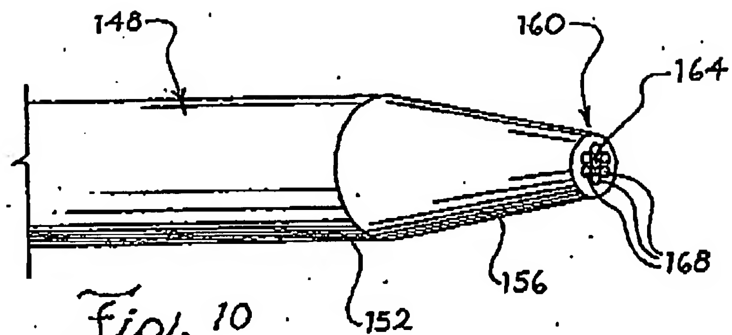
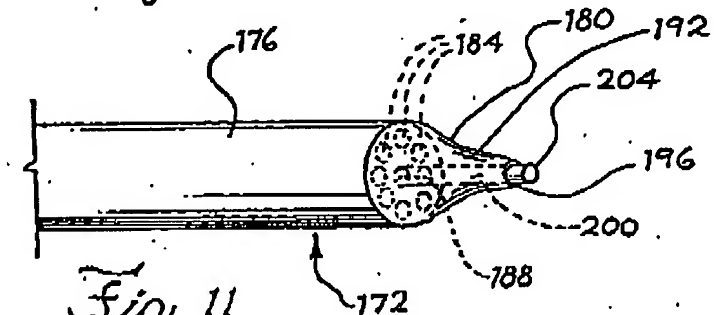


Fig. 10



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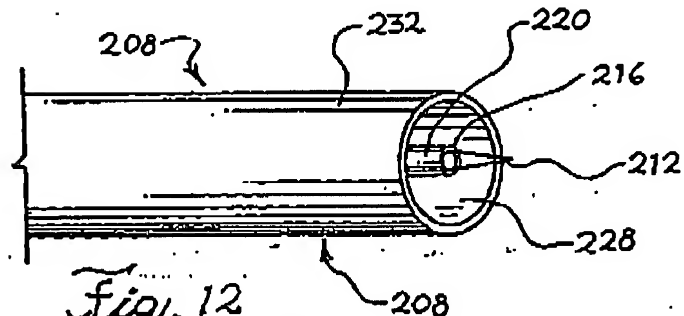


Fig. 12

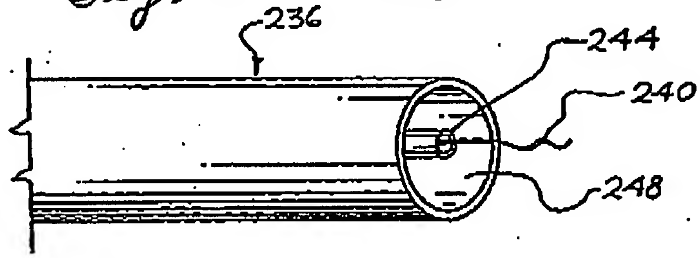


Fig. 13

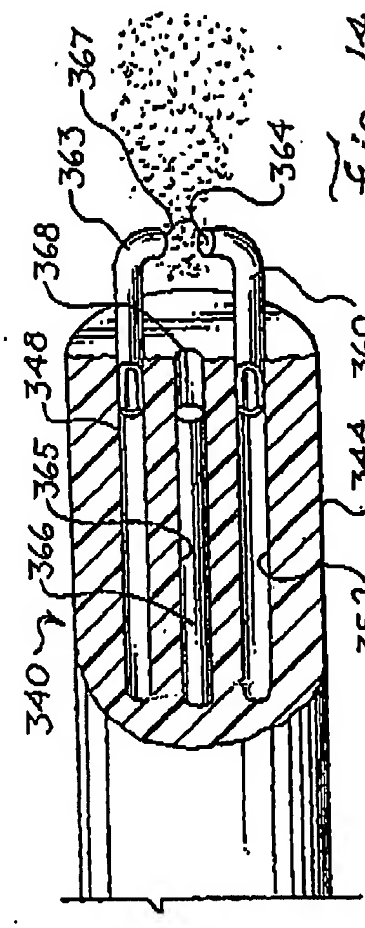
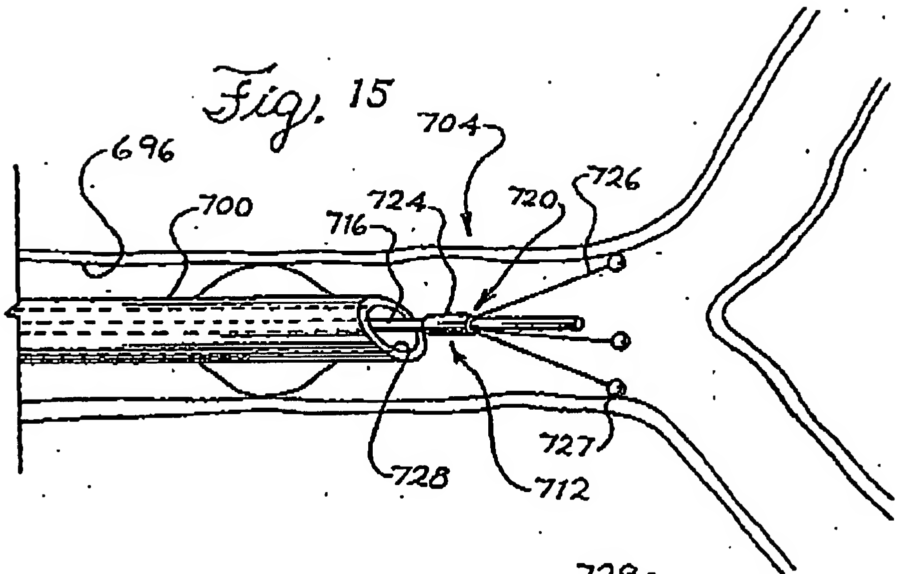
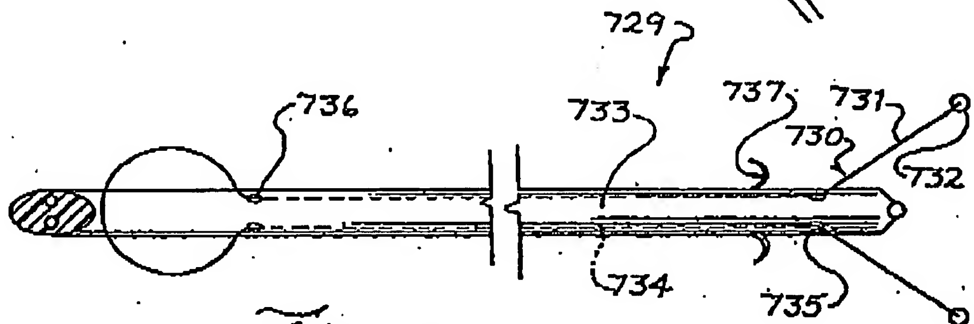


Fig. 14

Fig. 15





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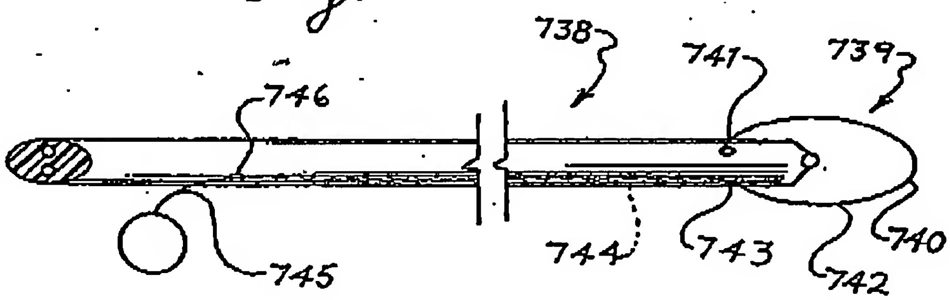
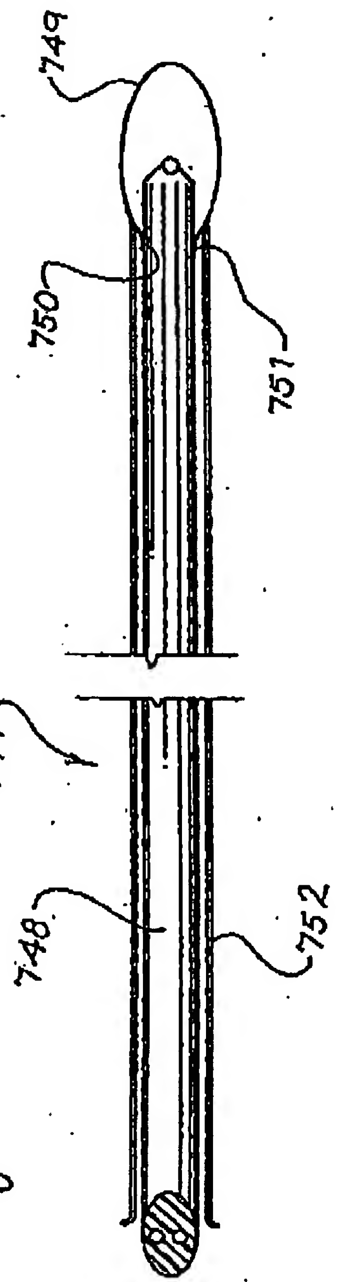


Fig. 17



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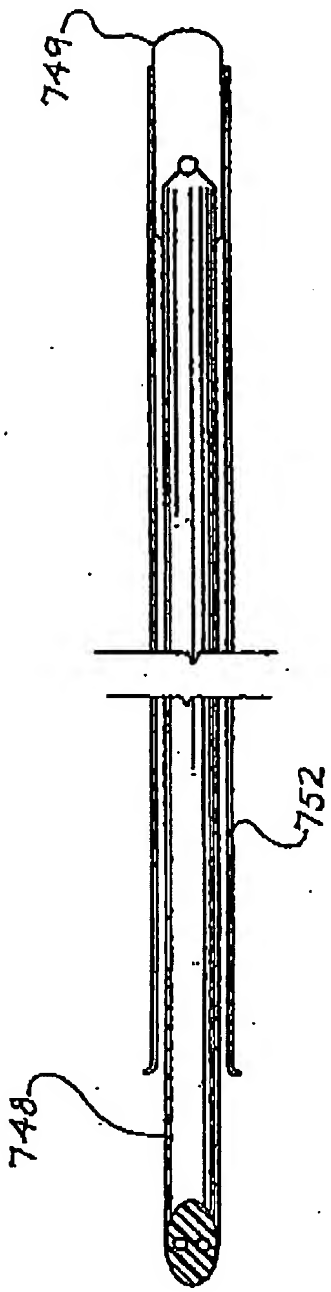
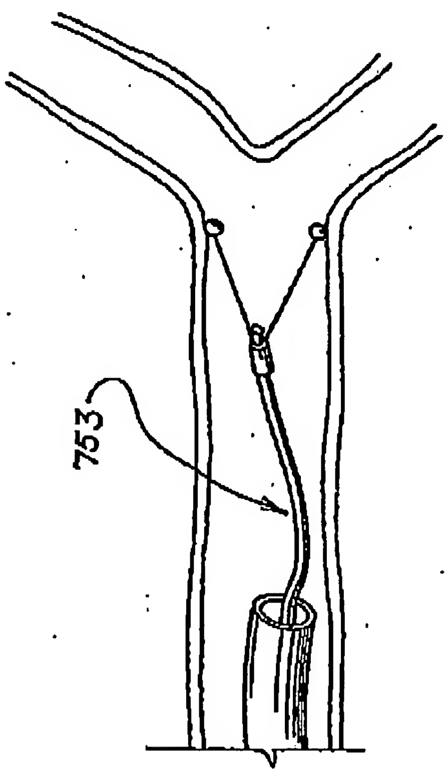
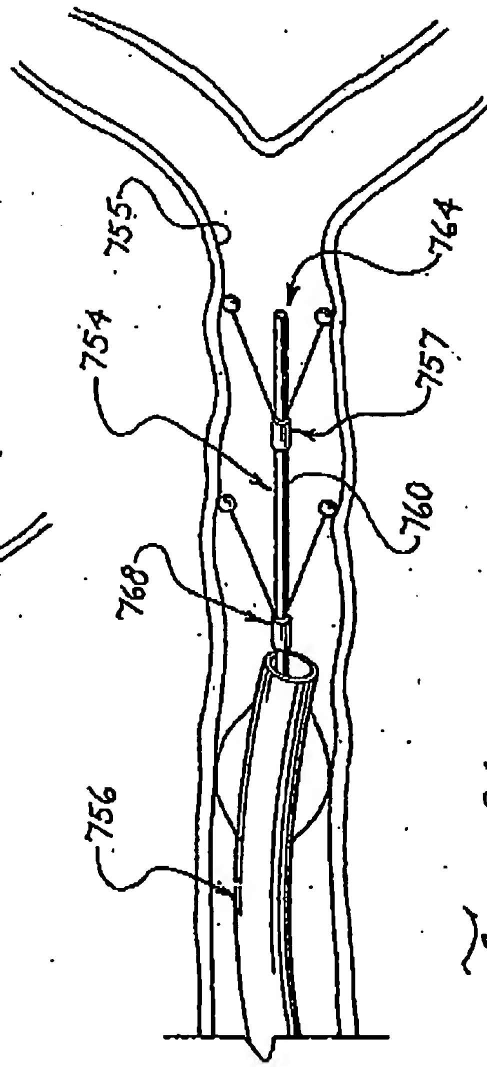


Fig. 19

Fig. 20





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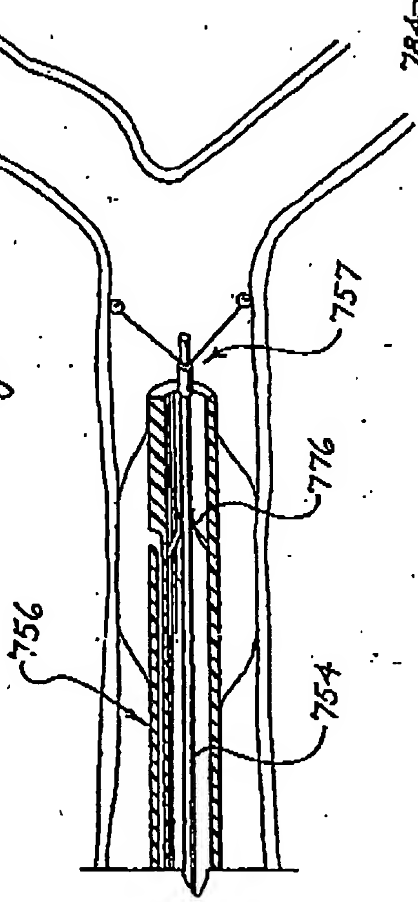


Fig. 22

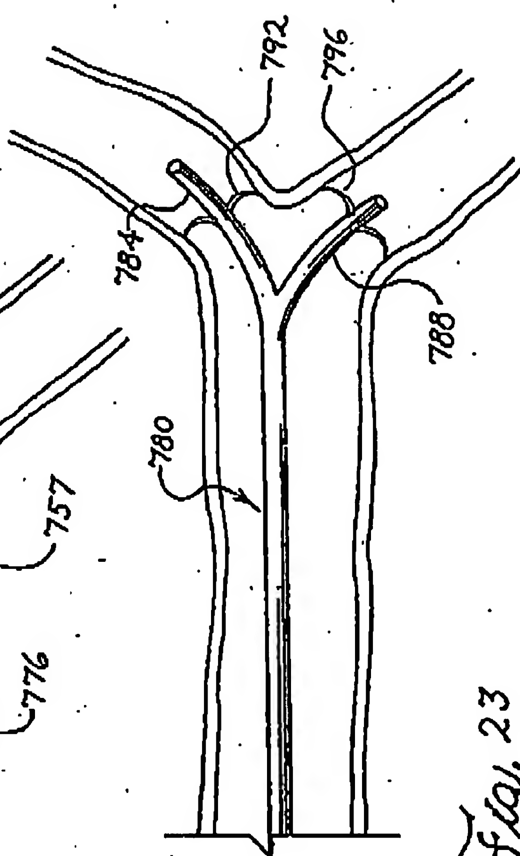


Fig. 23

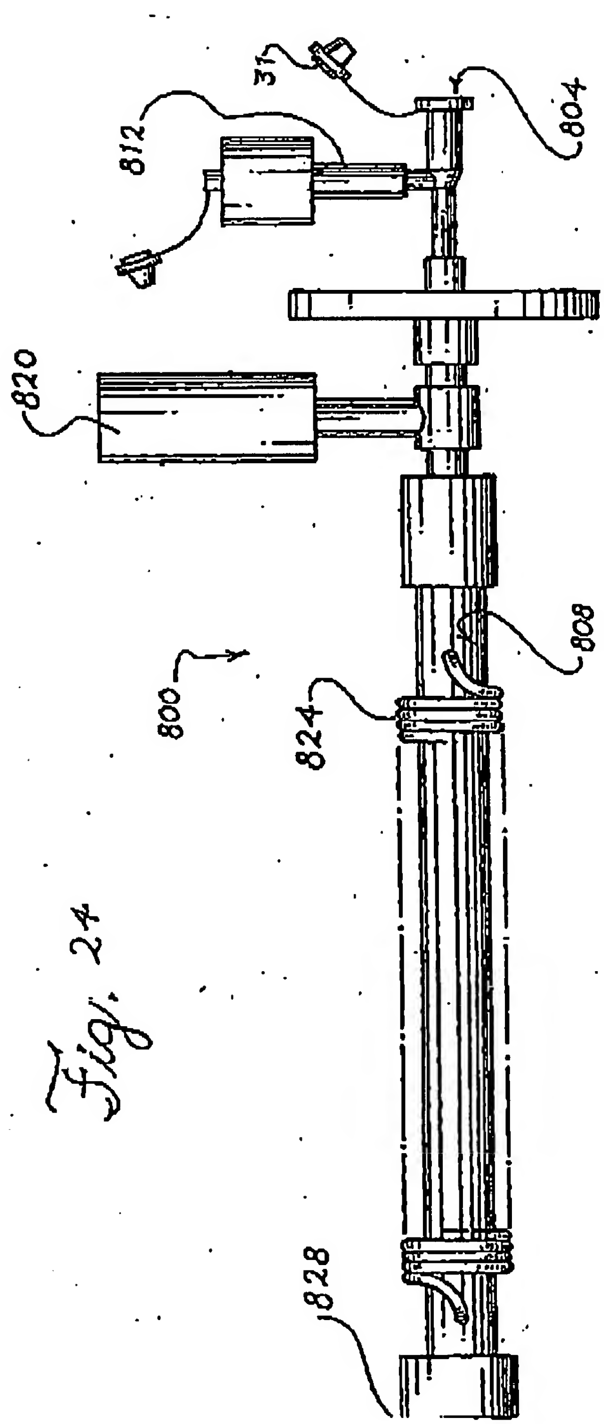


Fig. 24

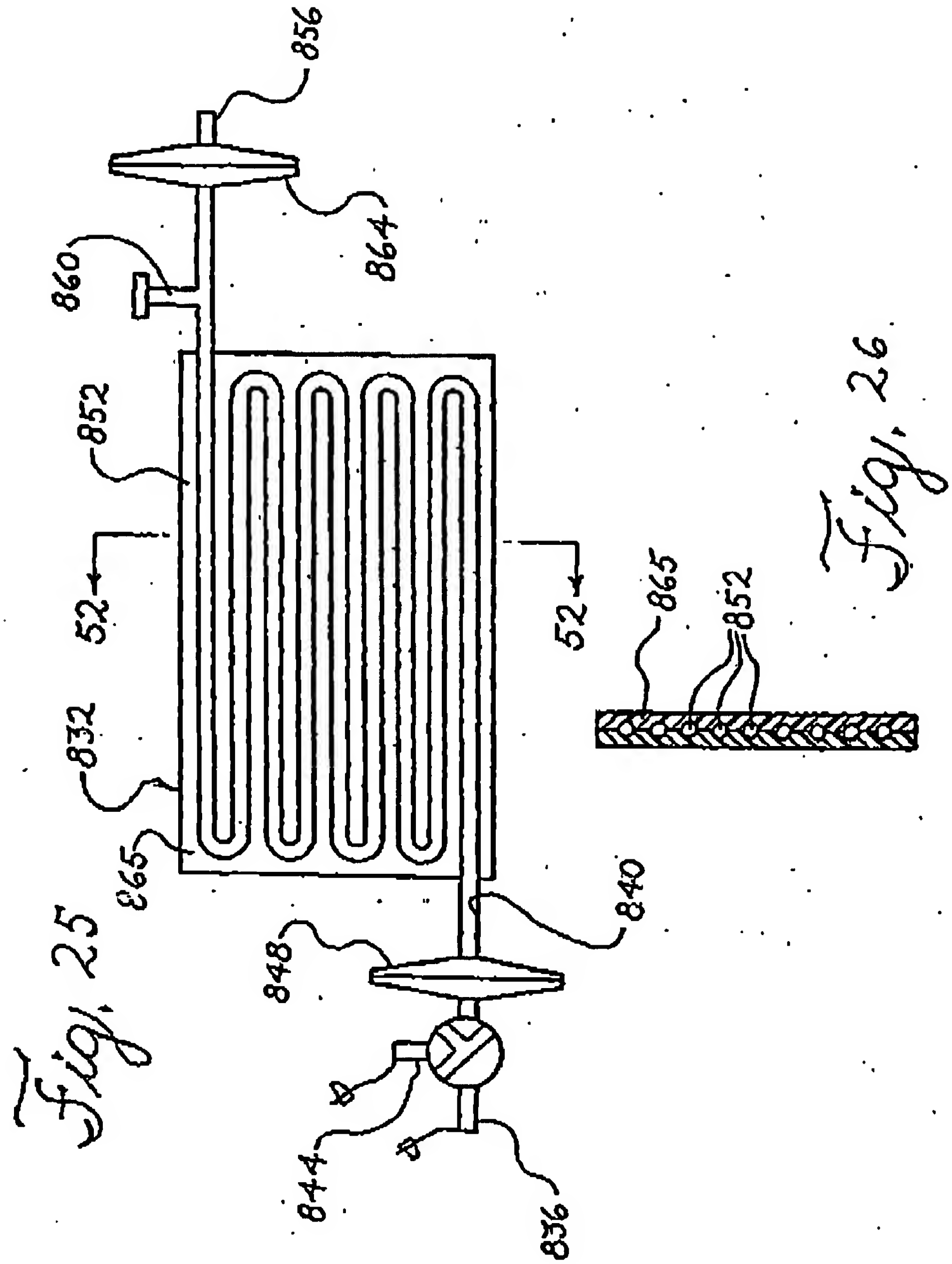


Fig. 25

Fig. 26

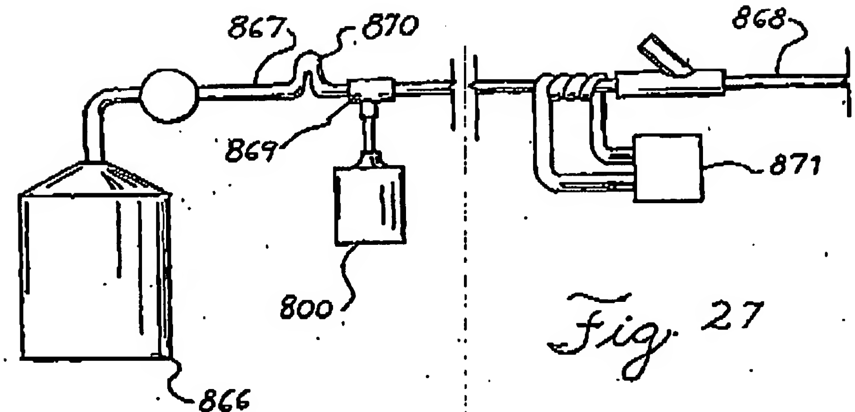
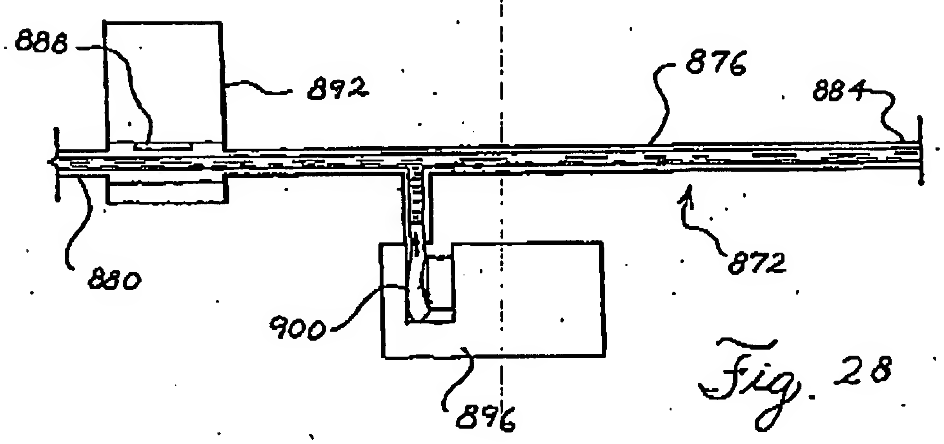


Fig. 27



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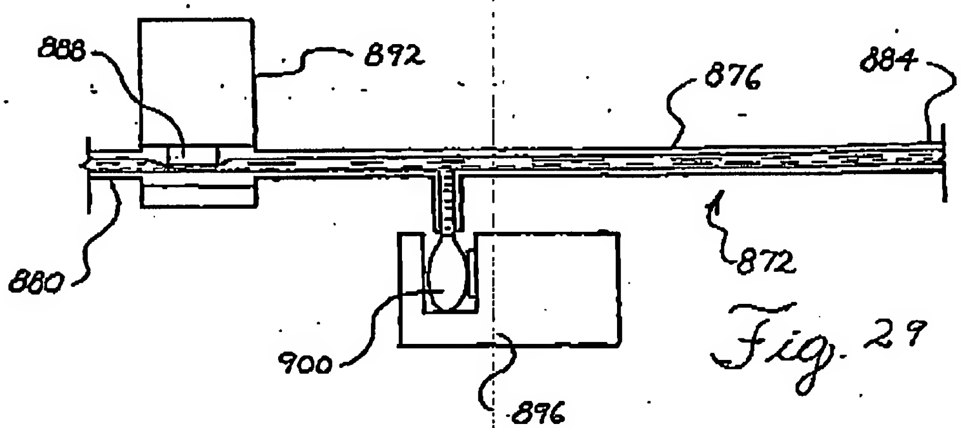
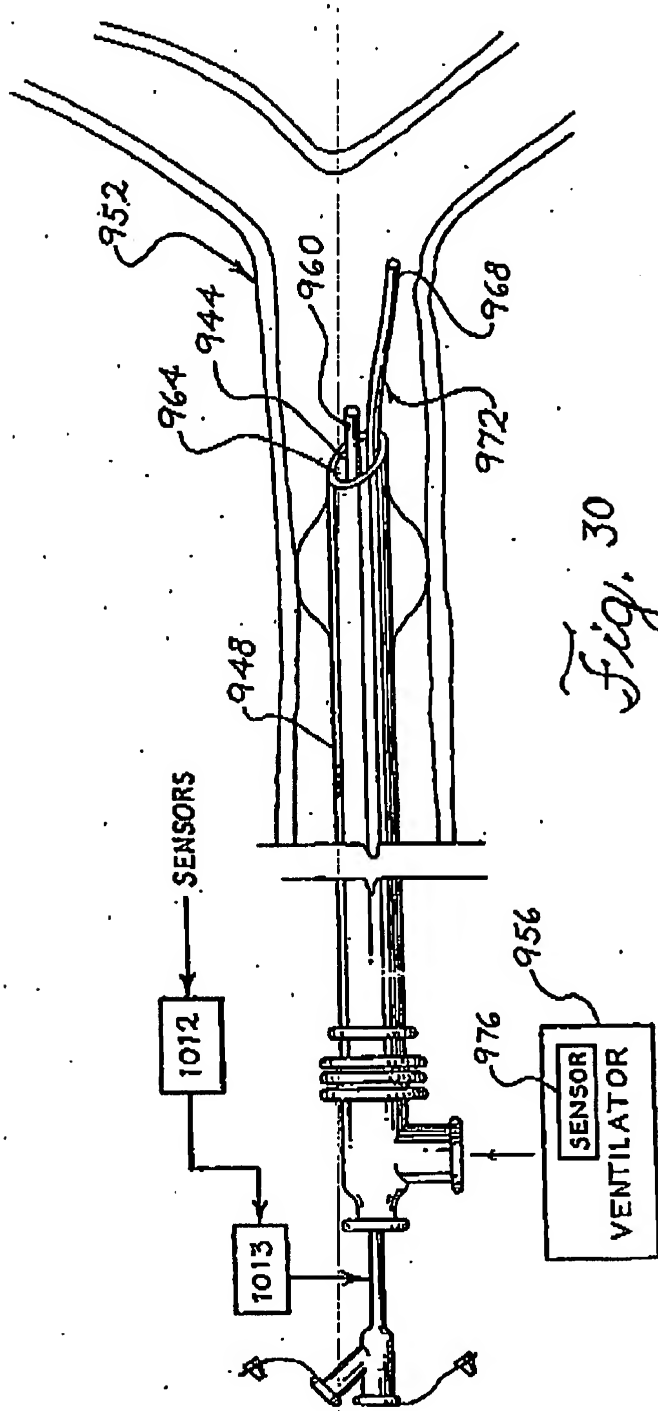


Fig. 29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SENSOR
VENTILATOR
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Fig. 30

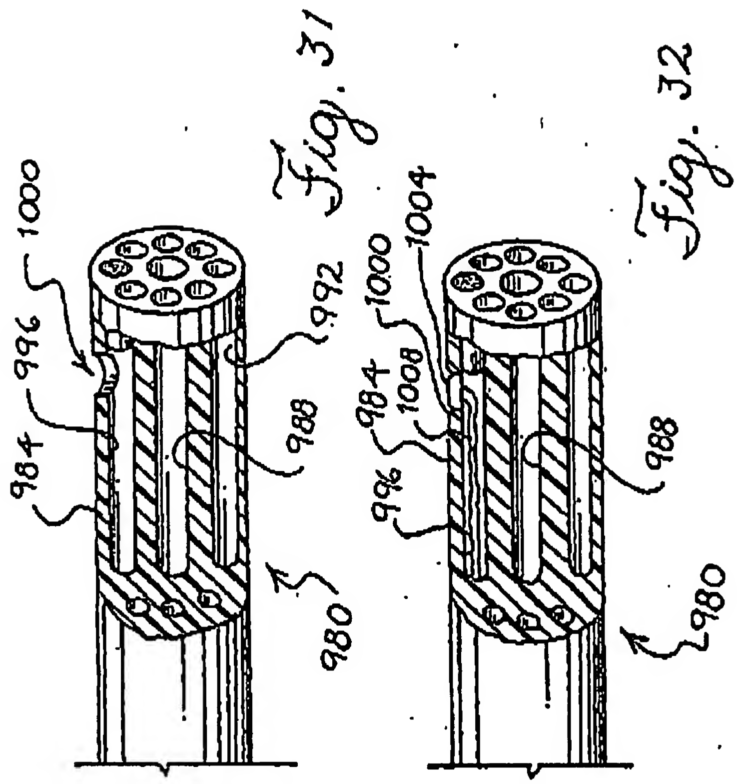

Fig. 31

Fig. 32

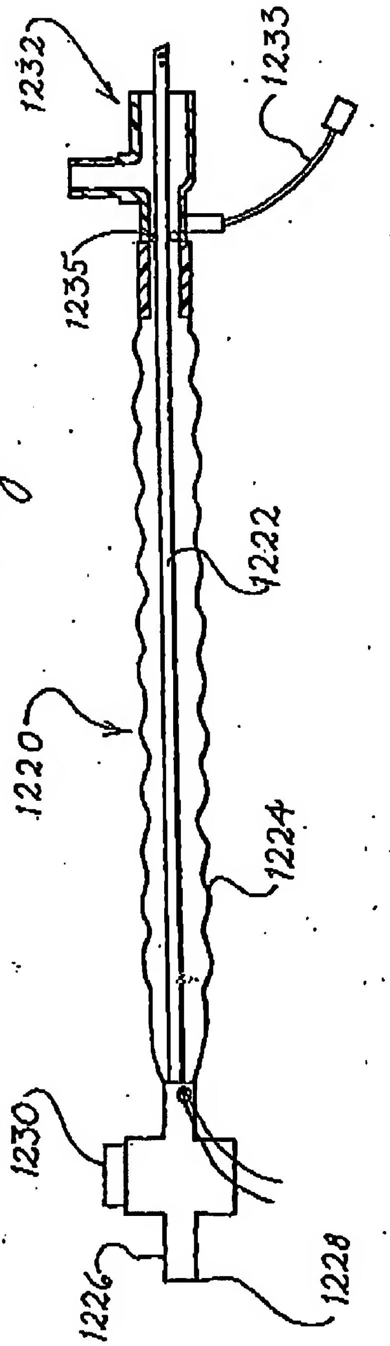
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Fig. 33

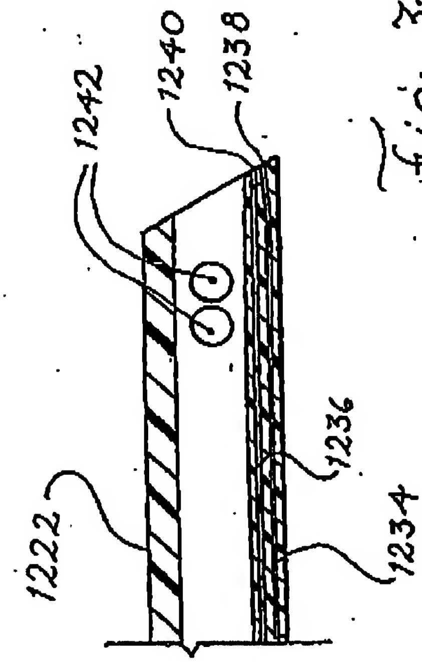
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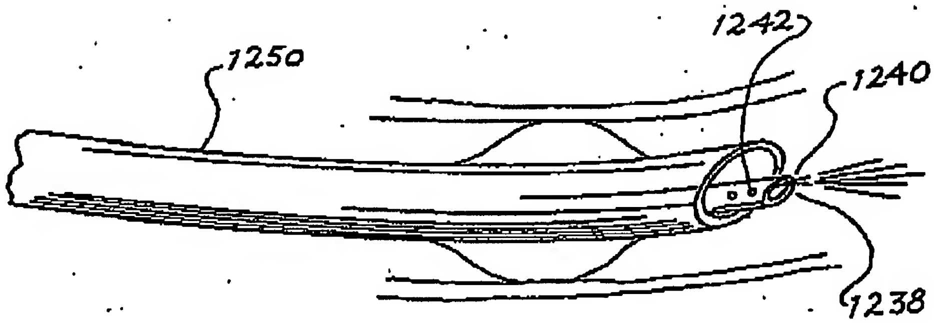
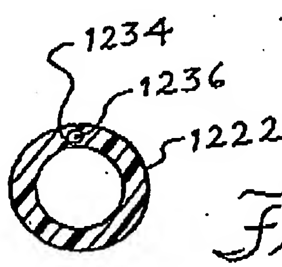
Fig. 34

Fig. 35





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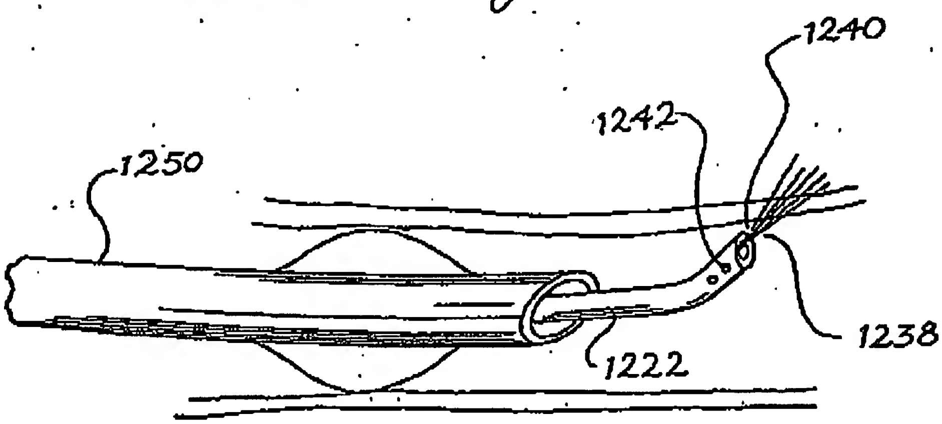
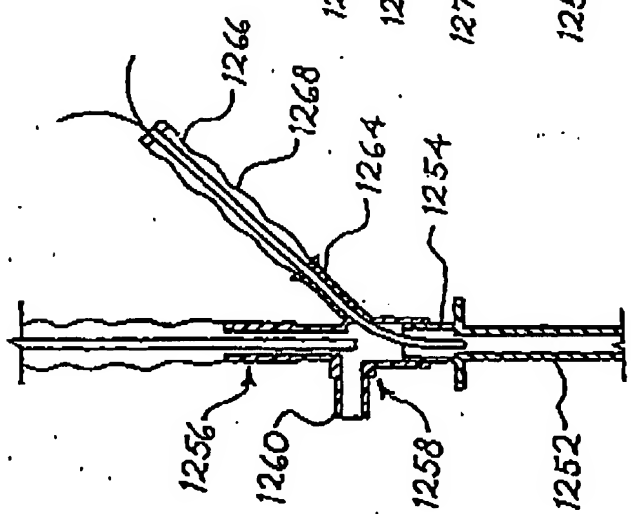


Fig. 37



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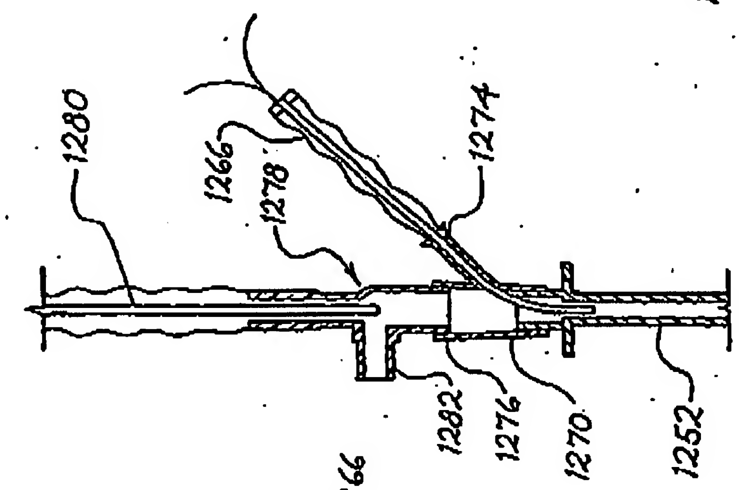

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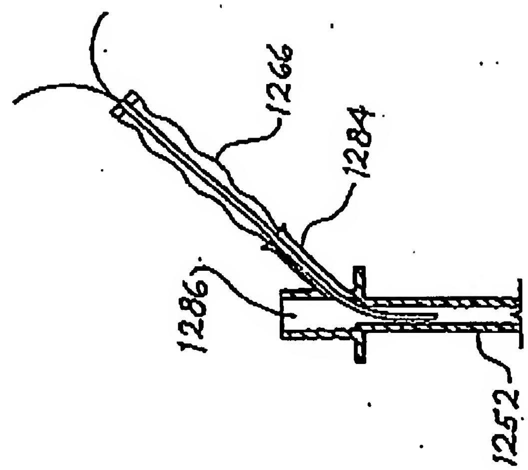

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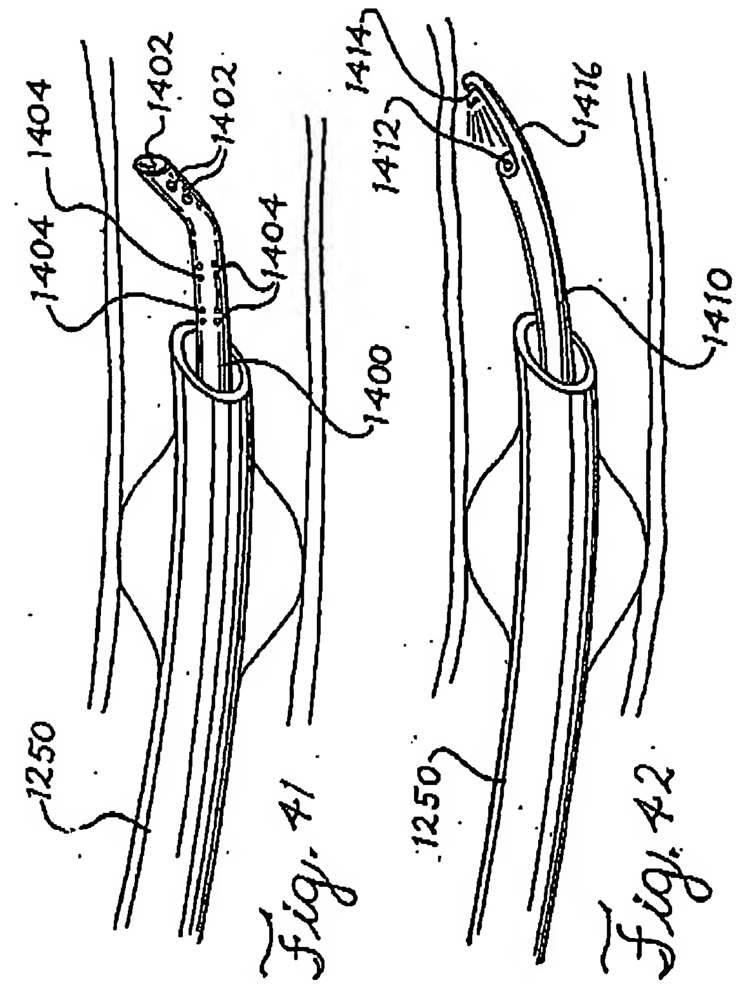
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Fig. 41

Fig. 42